Supporting Information

Osmylation of 10. rac-(3*R*, 4*S*)-3,4-Dihydroxy-*N*,*N*-diisopropyl-2-methylbutyramide (14a). To a solution of **10**[19] (97 mg, 0.53 mmol) in 1.0 mL CH_2Cl_2 was added TMEDA (93 μL, 0.62 mmol, 1.2 equiv) and the mixture was cooled to -78 °C. To this solution was added dropwise a solution of OsO_4 (160 mg, 0.62 mmol, 1.2 equiv) in CH_2Cl_2 (2x0.5 mL) and the dark colored reaction was stirred for 2 h at -78 °C. After evaporation of the solvent under an N_2 stream, 7 mL THF, 0.5 mL water and 1 g $NaHSO_3$ was added and the solution was heated to reflux for 2.5 h. After filtration through Celite and washing with ether, the filtrate was dried ($MgSO_4$) and evaporated to give 101 mg of **14a** (87%), >90% diols by ^{1}H NMR assay. The diastereomer ratio for the osmylation of **10** was not measurable from the mixture of diols, but acetonide formation (**18a** and **18b**) facilitated measurement of the ratio. Acetonide formation on 40 mg of **14a** afforded 40 mg (84%) of the crude acetonides, **18a** and **18b**, which were in a ratio of 19:1 by ^{1}H NMR assay (comparison of doublets of quartets at δ 2.91 (major) and δ 2.66 (minor). The balance of the material (61 mg) was purified by flash chromatography on EM silica gel 60 (7x1 cm, 2 mL fractions, fractions 7-12, 48 mg of **14a** (69%)), EtOAc eluent; analytical tlc on EM silica gel 60, EtOAc, Rf= 0.18. Molecular ion calcd for $C_{11}H_{23}NO_3$: 217.16780; found m/e= 217.1673, error= 2 ppm; IR (neat, cm^{-1}) 3402, O-H; 1608, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 4.85 (1H, br s) 4.00 (1H, sept, J= 7.0 Hz) 3.77-3.70 (1H, m) 3.66-3.49 (3H, m) 2.77 (1H, qd, J= 7.0, 4.8 Hz) 2.30 (1H, br s) 1.41-1.34 (6H, m) 1.28-1.20 (9H, m). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 175.8 s, 75.0 d, 65.1 t, 48.4 d, 46.0 d, 37.5 d, 21.0 q, 21.0 q, 20.5 q, 20.4 q, 15.5 q.

Acetonides 18a (major) and 18b (minor) from 14a.

The characterization samples were prepared from a sample of diols made at rt. To the crude osmylation product (**14a** and minor diastereomer, 5:1 dr) (25 mg, 0.12 mmol, from the NMO catalyzed osmylation of **10** at rt) was added 1 mg of camphor sulfonic acid and 1 mL of 2,2-dimethoxy propane and the solution was stirred for 4 h. After removal of the excess 2,2-dimethoxy propane (aspirator), the residue was purified by silica plug filtration (ether eluent) to afford 26 mg of **18a** and **18b** (86 %). ^{1}H NMR analysis of this material showed a 5.2:1 ratio of diastereomers. Pure material was obtained by preparative layer chromatography on EM silica gel 60 (20x10x0.01 cm) which yielded 20 mg **18a** (68%) and 4 mg **18b** (13%), 7:3 hexane/EtOAc eluent; analytical tlc on EM silica gel 60, 1:1 hexane/EtOAc. **18a (major diastereomer). rac-(3*R*, 4*S*)-3,4-dihydroxy-*N*,*N*-diisopropyl-2-methylbutyramide acetonide.** Colorless oil; Rf= 0.49. Molecular ion calcd for $C_{14}H_{27}NO_3$: 257.19910; found m/e= 257.1985, error= 2 ppm; IR (neat, cm^{-1}) 1635, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 4.32 (1H, q, J= 6.6 Hz) 4.11 (1H, dd, J= 8.5, 6.6 Hz) 4.14-4.01 (1H, m) 3.81 (1H, dd, J= 8.5, 6.6 Hz) 3.56 (1H, br s) 2.91 (1H, dq, J= 6.9, 6.9 Hz) 1.41 (3H, s) 1.38-1.33 (9H, m) 1.24-1.21 (6H, m) 1.07 (3H, d, J= 6.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 173.4 s, 108.3 s, 77.2 d, 66.9 t, 48.0 d, 45.7 d, 40.8 d, 26.5 q, 25.0 q, 21.3 q, 21.3 q, 20.8 q, 20.6 q, 12.8 q. **18b (minor diastereomer). rac-(3*R*, 4*R*)-3,4-dihydroxy-*N*,*N*-diisopropyl-2-methylbutyramide acetonide.** Colorless oil; Rf= 0.57. Molecular ion calcd for $C_{14}H_{27}NO_3$: 257.19910; found m/e= 257.1981, error= 4 ppm; base peak= 114 amu; IR (neat, cm^{-1}) 1633, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 4.33 (1H, dt, J= 8.5, 6.3 Hz) 4.13 (1H, dd, J= 8.5, 6.3 Hz) 4.01 (1H, sept, J= 6.6 Hz) 3.54 (1H, dd, J= 8.5, 5.9 Hz) 3.45 (1H, br s) 2.66 (1H, dq, J= 8.5, 7.0 Hz) 1.42 (3H, s) 1.37-1.34 (9H, m) 1.27-1.20 (9H, m).

Naproxen Ester 19. (2*S*, 2'*R*, 3'*S*)-2-(6-methoxynaphthalen-2-yl)-propionic acid 3'-(diisopropylcarbamoyl)-2'-hydroxybutyl ester.

To the diol **14a** (38 mg, 0.17 mmol, 7.5:1 dr), (*S*)-naproxen (44 mg, 0.19 mmol, 1.1 equiv, Syntex) and DMAP (2 mg, 0.02 mmol, 0.10 equiv) in 0.5 mL CH_2Cl_2 at 0 °C was added dimethylaminopropyl ethyl carbodiimide (40 mg, 0.21 mmol, 1.2 equiv) as a solid. After 1.5 h the reaction was diluted with CH_2Cl_2 (10 mL) and washed with water, then 1:1 water/sat'd $NaHCO_3$ (10 mL). Each of the aqueous layers was extracted with 3 mL CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and evaporated (aspirator) to an oil (70 mg, 94%). ^1H NMR analysis of the crude indicated a 1:1 mixture of diastereomers. A portion of the residue (57 mg) was purified by preparative layer EM silica gel 60 (20x20x0.1 cm) eluted twice, 3:1 hexane/ether eluent; analytical tlc on EM silica gel 60, 1:1 hexane/ether, Rf= 0.17 to afford **19** (16 mg, 28%) of a solid. A less polar diastereomer **20** (16 mg, 28%) did not crystallize and was not characterized. X-ray quality material (**19**) was obtained by crystallization from ether/hexane, mp 87.0-88.0 °C. Molecular ion calcd for $C_{25}H_{35}NO_5$: 429.25150; found m/e= 429.2491, error= 5 ppm; IR (neat, cm^{-1}) 3373, O-H; 1736, C=O; 1606, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 7.70 (1H, d, J= 8.7 Hz) 7.69 (1H, d, J= 8.7 Hz) 7.63 (1H, br s) 7.36 (1H, dd, J= 8.4, 1.8 Hz) 7.15 (1H, dd, J= 9.0, 2.5 Hz) 7.13 (1H, d, J= 2.7 Hz) 4.34 (1H, dd, J= 11.1, 5.1 Hz) 3.96-3.83 (5H, m) 3.76-3.71 (1H, m) 3.45-3.26 (2H, m) 2.38 (1H, dq, J= 6.9, 4.8 Hz) 1.55 (3H, d, J= 7.2 Hz) 1.32 (3H, d, J= 6.6 Hz) 1.28 (3H, d, J= 6.6 Hz) 1.03 (3H, d, J= 7.2 Hz) 0.94 (3H, d, J= 6.9 Hz) 0.9 (3H, d, J= 6.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 175.3 s, 174.3 s, 157.8 s, 136.1 s, 133.7 s, 129.2 d, 128.9 s, 127.2 d, 126.0 d, 125.9 d, 119.1 d, 105.6 d, 72.3 d, 66.3 t, 55.4 q, 48.5 d, 46.0 d, 45.6 d, 36.8 d,

29.7 q, 20.7 q, 20.6 q, 20.4 q, 18.8 q, 15.2 q.

Osmylation of 11. rac-(2*R*, 3*S*)-3,4-Dihydroxy-*N*,*N*-diisopropyl-2,3-dimethylbutyramide (15a). To a solution of **11**[19] (96 mg, 0.49 mmol) in 1.0 mL CH_2Cl_2 was added TMEDA (88 mL, 0.59 mmol, 1.2 equiv) and the mixture was cooled to -78 °C. To this solution was added OsO_4 (1.0 mL of a 0.59 M solution in CH_2Cl_2, 0.59 mmol, 1.2 equiv) and the dark colored reaction was stirred for 2 h at -78 °C. After evaporation of the solvent under an N_2 stream, 7 mL THF, 0.5 mL water and 1 g $NaHSO_3$ was added and the solution was heated to reflux for 2.5 h. After filtration through Celite and washing with ether, the filtrate was dried ($MgSO_4$) and evaporated to 98 mg of **15a** (94%). ^{1}H NMR analysis revealed a >20:1 diastereomer ratio and >95 % conversion to diol. The residue was purified by silica plug chromatography on EM silica gel 60 (2x1 cm) which yielded 92 mg **15a** (88%), EtOAc eluent; analytical tlc on EM silica gel 60, EtOAc, Rf= 0.40. Molecular ion calcd for $C_{12}H_{25}NO_3$: 231.18340; found m/e= 231.1832, error= 1 ppm; IR (neat, cm^{-1}) 3401, O-H; 1604, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 5.88 (1H, s) 4.04 (1H, sept, J= 6.3 Hz) 3.70-3.30 (3H, m) 2.64 (1H, q, J= 7.4 Hz) 2.30-2.20 (1H, m) 1.42-1.33 (6H, m) 1.27-1.19 (9H, m) 1.18 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 177.2 s, 73.7 s, 69.7 t, 48.7 d, 46.0 d, 39.2 d, 21.8 q, 20.9 q, 20.7 q, 20.4 q, 20.4 q, 12.5 q. The minor diol **15b** could not be isolated free of **15a**. Its presence was inferred from signals at δ 5.0, 3.65, 2.85, which were used as the basis for diastereomer assay by integration.

Osmylation of 12. rac-(2*R*,3*S*,4*S*)-3,4-Dihydroxy-*N*,*N*-diisopropyl-2,3-dimethylpentanamide (16a). To a solution of **12**[1] (120 mg, 0.569 mmol) in 1.0 mL CH_2Cl_2 was added TMEDA and the mixture was cooled to -78 °C. To this solution was added OsO_4 (0.68 mL, 1.26 M in

CH_2Cl_2, 1.5 equiv) and the dark colored reaction was stirred for 2 h at -78 °C and then warmed to rt. After addition of 10 mL of a 1:1 saturated $NaHSO_3$/THF solution, the reaction was heated to reflux for 1 h. To this was added 10 mL brine and the resulting solution was continuously extracted with EtOAc for 4 h. After the organic extracts were dried ($MgSO_4$) and evaporated (aspirator), the residue (127 mg, 91%) was analyzed by ^1H NMR to be 11:1 dr, >90% conversion to diols. Pure material was obtained by purification of one fifth of the initial product (25mg) on a preparative layer, EM silica gel 60 (20x10x0.01 cm) which yielded 20 mg (80%) **16a**, EtOAc eluent; analytical tlc on EM silica gel 60, EtOAc, Rf= 0.59. Molecular ion calcd for $C_{13}H_{27}NO_3$: 245.19910; found m/e= 245.1976, error= 6 ppm; base peak= 200 amu; IR (neat, cm^{-1}) 1604, C=O; 3442, O-H; 3263, O-H; 300 MHz NMR ($CDCl_3$, ppm) δ 6.26 (1H, s) 4.06 (1H, sept, J= 6.6 Hz) 3.69 (1H, q, J= 6.6 Hz) 3.41 (1H, sept, J= 6.6 Hz) 2.98 (1H, s) 2.61 (1H, q, J= 7.0 Hz) 1.40 (6H, d, J= 7.0 Hz) 1.30-1.20 (9H, m) 1.08 (3H, d, J= 6.6 Hz) 1.05 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 177.0 s, 76.7 s, 71.5 d, 49.0 d, 46.3 d, 38.4 d, 21.1 q, 20.9 q, 20.6 q, 20.4 q, 17.3 q, 17.1 q, 12.9 q. The minor diol **16b** could not be isolated free of **16a**. Its presence was inferred from signals at δ 3.9 and 2.7, which were used as the basis for diastereomer assay by integration.

Osmylation of 13. rac-(2*R*, 3*R*, 4*S*)-3,4-Dihydroxy-*N*,*N*-diisopropyl-2,3-dimethylpentanamide (17b). To a solution of **13**[1] (48 mg, 0.227 mmol, contaminated with 8 % **12**) in 1.0 mL CH_2Cl_2 was added TMEDA and the mixture was cooled to -78 °C. To this solution was added OsO_4 (0.68 mL, 1.26 M in CH_2Cl_2, 1.5 equiv) and the dark colored reaction was stirred for 2 h at -78 °C and then warmed to rt and the solvent was removed under N_2. After 10 mL of a 1:1 saturated $NaHSO_3$/THF solution was added, the reaction was heated to reflux for 1 h. To this

was added 10 mL brine and the resulting solution was continuously extracted with EtOAc for 4 h. After the organic extracts were dried ($MgSO_4$) and solvent removed (aspirator), the residue was analyzed by ^1H NMR to be >20:1 dr (**17b/17a**) with 7 % of the diol **16a** from the alkene isomer **12**, >95% conversion to diols. One third of the residue was purified by preparative layer EM silica gel 60 (20x10x0.01 cm) to yield 13 mg (71%) of **17b**, 1:1 ether/CH_2Cl_2 eluent; analytical tlc on EM silica gel 60, 1:1 ether/CH_2Cl_2, Rf= 0.45. Molecular ion calcd for $C_{13}H_{27}NO_3$: 245.19910; found m/e= M+1, 246.2060, error= 4 ppm; IR (neat, cm^{-1}) 3421, O-H; 1606, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 6.02 (1H, s) 4.15-3.95 (1H, m) 3.83 (1H, q, J= 6.6 Hz) 3.75-3.50 (1H, m) 2.93 (1H, q, J= 7.1 Hz) 2.12 (1H, br s) 1.42-1.35 (6H, m) 1.28-1.20 (12H, m) 1.10 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 177.8 s, 74.5 s, 71.3 d, 48.6 d, 46.0 d, 39.1 d, 22.1 q, 21.3 q, 21.1 q, 20.5 q, 20.2 q, 17.0 q, 15.2 q.

Osmylation of 13 using the NMO procedure. rac-(2*R*, 3*S*, 4*R*)-3,4-Dihydroxy-*N*,*N*-diisopropyl-2,3-dimethylpentanamide (17a). The general NMO osmylation procedure was performed at 0 °C using **13**[1] (104 mg, 0.49 mmol). ^1H NMR assay of the crude product (100 mg, 82%) indicated a 7:1 diastereomeric ratio (**17b**:**17a**) with 10% of **16a** from the alkene geometrical isomer **12**. A portion of the crude residue (90 mg) was purified by flash chromatography on EM silica gel 60 (19x1.8 cm, 7 mL fractions; fractions 32-34 contained 7 mg (6%) **17a** (white solid); fractions 36-42 contained 81 mg (75%) **17b** and **16a** (8:1 ratio)), 7:3 (150 mL) to 1:1 hexane/EtOAc eluent. Pure **17a** and X-ray quality crystals were obtained by crystallization from ether/hexane, mp 110.5-111.5 °C. Analytical tlc on EM silica gel 60, 7:3 hexane/EtOAc, Rf= 0.27; Molecular ion calcd for $C_{13}H_{27}NO_3$: 245.19910; found m/e= 246.2070, error= 0 ppm; IR (neat, cm^{-1}) 3396, O-H; 1599, C=O; 300 MHz NMR ($CDCl_3$,

ppm) δ 4.19 (1H, sept, J= 6.6 Hz) 3.71 (1H, q, J= 6.2 Hz) 3.43 (1H, sept, J= 7.0 Hz) 2.98 (1H, q, J= 7.1 Hz) 1.44-1.36 (6H, m) 1.27-1.16 (12H, m) 1.05 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 178.0 s, 75.6 s, 73.3 d, 49.0 d, 46.1 d, 37.7 d, 21.0 q, 20.7 q, 20.6 q, 20.5 q, 18.4 q, 18.1 q, 13.0 q.

Lactonization of 15a. rac-(3*R*, 4*S*)-4-Hydroxy-3-methyldihydrofuran-2-one (21). To **15a** (92 mg, 0.40 mmol) was added 1.1 mL of a 10% H_2SO_4 solution (v/v) and the mixture was heated to 100 °C for 3 h. The acid layer was extracted with ether (8 x 3 mL). The organic layer was dried ($MgSO_4$) and evaporated (aspirator) to give 43 mg (84%) of crude **21** containing ca. 5% elimination product by ^1H NMR assay. Half of the initial product (22 mg) was purified by preparative layer chromatography on EM silica gel 60 (20x10x0.01 cm) which yielded 18 mg (69%) **21**, EtOAc eluent; analytical tlc on EM silica gel 60, EtOAc, Rf= 0.51. Molecular ion calcd for $C_6H_{10}O_3$: 130.06290; found m/e= 130.0638, error= 6 ppm; IR (neat, cm^{-1}) 3460, O-H; 1755, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 4.24 (1H, d, J= 9.9 Hz) 4.07 (1H, d, J= 9.6 Hz) 2.42 (1H, q, J= 7.0 Hz) 1.81 (1H, s) 1.43 (3H, s) 1.23 (3H, d, J= 7.0 Hz).

Lactonization of 16a. rac-(3*R*, 4*S*, 5*S*)-4-Hydroxy-3,4,5-trimethyldihydrofuran-2-one (22). To **16a** (10 mg, 0.04 mmol) was added 0.12 mL of 10% H_2SO_4 solution (v/v) and the mixture was heated to 100 °C for 1.5 h. The acid layer was extracted with ether (3 x 5 mL). The organic layer was dried ($MgSO_4$) and evaporated (aspirator) to give 5.5 mg **22** (91%) containing ca. 6% elimination product by ^1H NMR assay. Pure material was obtained by preparative layer chromatography on EM silica gel 60 (20x10x0.01 cm) which yielded 4 mg (60%) of **22**, 4:1 CH_2Cl_2/ether eluent, eluted twice; analytical tlc on EM silica gel 60, 4:1 CH_2Cl_2/CH_2Cl_2, Rf= 0.29. Molecular ion calcd for $C_7H_{12}O_3$: 144.07860; found m/e= 144.0787, error= 1 ppm; IR

(neat, cm^{-1}) 3450, O-H; 1757, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 4.29 (1H, q, J= 6.5 Hz) 2.49 (1H, q, J= 7.1 Hz) 1.40 (1H, s) 1.39 (3H, d, J= 6.6 Hz) 1.33 (3H, s) 1.22 (3H, d, J= 7.0 Hz).

Lactonization of 17b. rac-(3*R*, 4*R*, 5*S*)-4-Hydroxy-3,4,5-trimethyldihydrofuran-2-one (23). To **17b** (53 mg, 0.22 mmol) was added 0.59 mL of 10% H_2SO_4 solution (v/v) and heated to 100 °C for 1 h. The acid layer was extracted with ether (4 x 3 mL). The organic layer was dried ($MgSO_4$) and evaporated (aspirator) to give 31 mg **23** (95%) containing ca. 3% elimination product by ^1H NMR assay. Pure material was obtained by preparative layer chromatography on EM silica gel 60 (20x10x0.01 cm) which yielded 10 mg **23** (64%), 1:1 hexane/EtOAc eluent; analytical tlc on EM silica gel 60, 1:1 hexane/EtOAc, Rf= 0.26. Molecular ion calcd for $C_7H_{12}O_3$: 144.07860; found m/e= 144.0787, error= 1 ppm; IR (neat, cm^{-1}) 3431, O-H; 1750, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 4.31 (1H, q, J= 6.6 Hz) 2.72 (1H, q, J= 7.1 Hz) 1.70 (1H, s) 1.35 (3H, d, J= 6.2 Hz) 1.19 (3H, d, J= 7.0 Hz) 1.14 (3H, s).

rac-(1*R*, 2*S*, 3*R*)-2,3-Dihydroxy-*N*,*N*-diisopropyl-3-methylcyclohexane carboxamide (25). The title compound was prepared according the general NMO mediated osmylation procedure. Reaction parameters: 37 mg alkene **24**[9] (0.166 mmol), 29 mg NMO (0.25 mmol), 60 μL of a 2.5% v/v OsO_4 solution in *t*-BuOH (0.02 equiv), rt. The residue (41 mg, 95%) was found to be a single isomer (>20:1) by ^1H NMR. Pure material was obtained by plug filtration chromatography on EM silica gel 60 (2x1 cm) which yielded 38 mg (88%) **25** as a white solid, 1:1 hexane/EtOAc eluent. Recrystallization from hexane gave white crystals, mp 129.0-129.5 °C; analytical tlc on EM silica gel 60, 1:1 hexane/EtOAc, Rf= 0.32. Molecular ion calcd for $C_{14}H_{27}NO_3$: 257.19910; found m/e= 257.1986, error= 2 ppm; IR (neat, cm^{-1}) 3380, O-H;

1619, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 4.06 (1H, sept, J= 6.6 Hz) 3.8 (1H, d, J= 9.6 Hz) 3.50 (1H, br s) 2.89 (1H, br s) 2.82 (1H, ddd, J= 12.5, 9.6, 3.7 Hz) 2.20 (1H, br s) 1.86-1.77 (1H, m) 1.76-1.58 (2H, m) 1.54-1.44 (1H, m) 1.43-1.33 (8H, m) 1.30 (3H, s) 1.24 (3H, d, J= 6.6 Hz) 1.21 (3H, d, J= 6.6 Hz). ^{13}C NMR (75 MHz, DEPT 90, DEPT 135, $CDCl_3$, ppm) δ 173.9 s, 75.8 d, 71.5 s, 48.0 d, 45.8 d, 45.3 d, 37.1 t, 28.6 t, 27.7 q, 21.2 q, 21.1 q, 20.8 t, 20.7 q, 20.6 q.

Osmylation of ethyl 2-(1-cyclohexenyl)propionate 26.[20]

To a solution of **26**[20] (140 mg, 0.79 mmol) and TMEDA (0.14 mL, 0.94 mmol) in 2.0 mL CH_2Cl_2 at -78 °C was added dropwise a solution of OsO_4 (240 mg, 0.94 mmol) in CH_2Cl_2 (2 x 0.5 mL). After 30 min, tlc analysis indicated that **26** had been consumed. To reduce the osmate ester, 3-mercaptopropionic acid (0.8 mL) was added and the solution was stirred at rt for 30 min. The solution was filtered through a celite pad and CH_2Cl_2 (15 mL) was added. This solution was extracted with sat'd Na_2CO_3 (10 mL). The aqueous layer was then extracted with CH_2Cl_2 (2 x 15 mL). The combined organic layers were dried ($MgSO_4$) and evaporated (aspirator) to a black oil. The residue was purified by flash chromatography on EM silica gel 60 (13 x 1 cm, 45 mL then 8 mL fractions). Fractions 6-9, 83 mg contained the known diol[11] (83 mg, 50%), 1.2:1 isomer ratio according to ^1H NMR analysis.

Hydroboration of 12. rac-(2*R*, 3*S*, 4*R*)-4-Hydroxy-*N*,*N*-diisopropyl-2,3-dimethylpentanamide (27b). To **12** (87mg, 0.41 mmol) was added 9-BBN (2.1 mL, 1.0 mmol, 0.5 M in THF) and the solution was heated to reflux for 4 h. After cooling to rt, 0.5 mL ethanol, 0.5 mL 3N NaOH and 0.5 mL 30% H_2O_2 were added sequentially and slowly while cooling with a water bath. This solution was stirred for 3 h. Water (10 mL) was added and the biphasic solution was

extracted with ether (3 x 50 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated (aspirator). The residue was purified by flash chromatography on EM silica gel 60 (13 x 1.5 cm, 75 mL prerun, 10 mL fractions, fractions 9-14 contained alcohol products, 70 mg (74%) with a diasteromer ratio of 5.7:1 by ^1H NMR), 7:3 (75 mL) to 1:1 hexane/EtOAc eluent; analytical tlc on EM silica gel 60, 1:1 hexane/EtOAc, Rf= 0.23.

Pure **27b** was obtained by derivatization with 3,5-dinitrobenzoyl chloride (pyridine, rt), followed by preparative layer chromatography on EM silica gel 60 (20x20x0.1 cm), 7:3 hexane/EtOAc eluent, Rf= 0.49. The DNB ester was cleaved using NaOH in MeOH to afford pure **27b**. Molecular ion calcd for $C_{13}H_{27}NO_2$: 229.20420; found m/e= 229.2049, error= 3 ppm; IR (neat, cm^{-1}) 3423, O-H; 1616, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 4.70 (1H, br s) 4.01 (1H, sept, J= 6.6 Hz) 3.75 (1H, dqd, J= 8.5, 6.0, 2.6 Hz) 3.58 (1H, br s) 2.65 (1H, qd, J= 7.0, 3.3 Hz) 1.76 (1H, dqd, J= 8.5, 7.0, 2.9 Hz) 1.36 (3H, br d, J= 6.6 Hz) 1.35 (3H, br d, J= 6.6 Hz) 1.27-1.23 (6H, m) 1.17 (3H, d, J= 7.0 Hz) 1.15 (3H, d, 6.0 Hz) 0.93 (3H, d, 7.0 Hz).

Hydroboration of 13. rac-(2*R*,3*S*,4*S*)-4-Hydroxy-*N*,*N*-diisopropyl-2,3-dimethylpentanamide (28b). To **13** (40 mg, 0.19 mmol, contaminated with 9% **12**) was added 9-BBN (2.0 mL, 1.0 mmol, 0.5 M in THF) and the solution was heated to reflux for 24 h. After cooling to rt, 1.0 mL ethanol, 2.0 mL 3N NaOH and 2.0 mL 30% H_2O_2 were added sequentially and slowly while cooling with a water bath. This solution was stirred for 3 h. Water (10 mL) was added and the biphasic solution was extracted with ether (3 x 30 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated (aspirator). ^1H NMR analysis of the crude indicated the presence of two alcohol products **28b** and **27b** in a 8.2:1 ratio. The minor diastereomer from

13 was not observed, and the diasteromer ratio was estimated to be at least 10 to 1. A fifth of the residue was purified by preparative layer chromatography on EM silica gel 60 (20x20x0.1 cm), 1:1 hexane/EtOAc eluent, to give 6 mg (70%) of an 8:1 mixture of **28b** and **27b** as a colorless oil; analytical tlc on EM silica gel 60, 1:1 hexane/EtOAc, Rf= 0.24.

Pure **28b** was obtained by derivatization with 3,5-dinitrobenzoyl chloride (pyridine, rt, 100%), followed by preparative layer chromatography on EM silica gel 60 (20x20x0.1 cm), 7:3 hexane/EtOAc eluent, Rf= 0.43. The DNB ester was cleaved using NaOH in MeOH to afford pure **27b** (100%). Molecular ion calcd for $C_{13}H_{27}NO_2$: 229.20420; found m/e= 229.2062, error= 9 ppm; base peak= 184 amu; IR (neat, cm^{-1}) 3417, O-H; 1614, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 4.20-4.05 (2H, m) 3.55 (1H, br s) 2.73 (1H, dq, J= 9.2, 7.0 Hz) 1.80 (1H, dqd, J= 9.2, 7.0, 2.2 Hz) 1.64 (1H, br s) 1.44-1.35 (6H, m) 1.26-1.19 (9H, m) 1.14 (3H, d, J= 7.0 Hz) 0.86 (3H, d, J= 7.0 Hz).

Hydroboration of 1. rac-(2*R*, 1'*S*, 2'*R*)-2-(2'-hydroxycyclohexyl)-*N*,*N*-diisopropylpropanamide. To **1** (103 mg, 0.43 mmol) was added 9-BBN (3.6 mL, 1.8 mmol, 0.5 M in THF) and the solution was heated to reflux for 24 h. After cooling to rt, 1.0 mL ethanol, 2.0 mL 3N NaOH and 2.0 mL 30% H_2O_2 were added sequentially and slowly while cooling with a water bath. This solution was stirred for 3 h. Water (10 mL) was added and the biphasic solution was extracted with ether (3 x 50 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated (aspirator). ^1H NMR analysis of this material indicated the presence of one diastereomer. The residue was purified by flash chromatography on EM silica gel 60 (15 x 1.5 cm, 60 mL prerun,10 mL fractions, fractions 2-3, 76 mg **29b**, (69%)), 1:1 hexane/EtOAc eluent; analytical tlc on EM silica gel 60, 1:1 hexane/EtOAc, Rf= 0.28.

Molecular ion calcd for $C_{15}H_{29}NO_2$: 255.21980; found m/e= 255.2203, error= 2 ppm; IR (neat, cm^{-1}) 3392, O-H; 3291, O-H; 1608, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 6.01 (1H, br s) 3.98 (1H, sept, J= 6.6 Hz) 3.65 (1H, br s) 3.49-3.39 (1H, m) 2.62 (1H, q, J= 7.2 Hz) 2.10-2.00 (1H, m) 1.70-1.61 (2H, m) 1.60-1.50 (2H, m) 1.42-1.15 (19H, m).

Correlation of 29b with the pinacol rearrangement product from 2b.

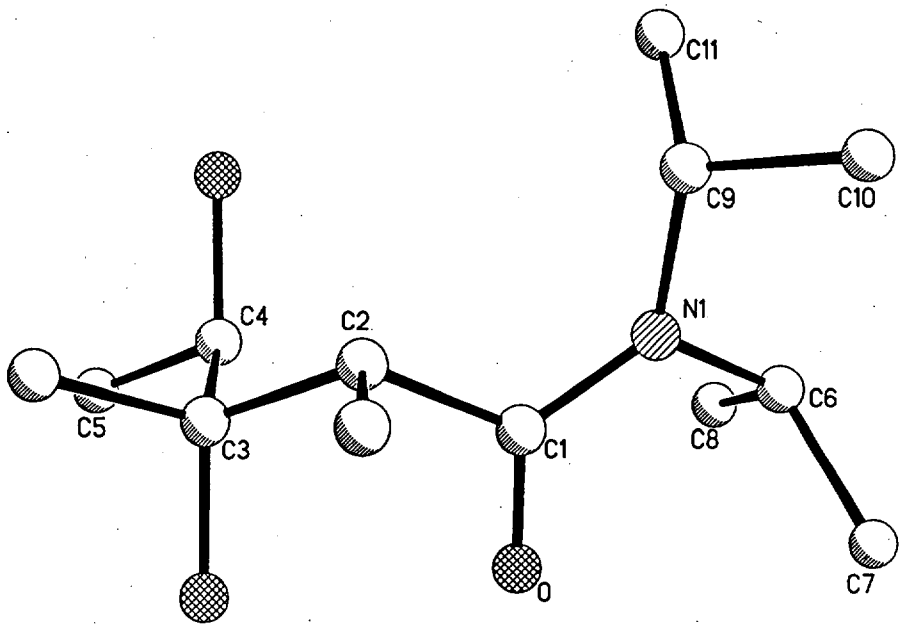
A solution of **29b** (15 mg) in CH_2Cl_2 (0.35 mL) was added at -78 °C to the Swern reagent prepared by slow addition of oxaloyl chloride (10.5 μL) to DMSO (16.8 μL) in 0.4 mL CH_2Cl_2. After 30 min, triethylamine (82 μL) was added dropwise. After 5 min, the reaction was allowed to warm to 0 °C (15 min) and then to rt (15 min). Ether (5 mL) was added and the organic phase was washed with sat'd $NaHCO_3$, dried ($MgSO_4$), and evaporated to an oil, single major product according to tlc analysis, 1:1 hexane/EtOAc, Rf= 0.47. The crude Swern product was treated with 25 mg K_2CO_3 and 1 mL MeOH and the solution was refluxed for 1 h. After filtration and solvent removal, the mixture (1:1 ratio of diastereomers by NMR assay) was purified by preparative layer chromatography on EM silica gel 60 (20x10x0.02 cm), 4:1 hexane/EtOAc eluent; analytical tlc on EM silica gel 60 to give two bands. The less polar was the recovered Swern product, 1:1 hexane/EtOAc, Rf= 0.47. Molecular ion calcd for $C_{15}H_{27}NO_2$: 253.20420; found m/e= 253.2041, error= 0 ppm; IR (neat, cm^{-1}) 1708, C=O; 1634, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 4.11 (1H, br s) 3.53 (1H, br s) 3.02 (1H, dq, J= 9.6, 6.6 Hz) 2.80-2.70 (1H, m) 2.45-2.31 (2H, m) 2.24-2.05 (2H, m) 1.84-1.60 (3H, m) 1.36 (6H, br d, J= 6.3 Hz) 1.26-1.16 (7H, m) 1.13 (3H, d, J= 6.6 Hz). The more polar zone (1:1 hexane/EtOAc, Rf= 0.40) was identical with the pinacol side product obtained from lactonization of **2b**; molecular ion calcd for $C_{15}H_{27}NO_2$: 253.20420; found m/e= 253.2064,

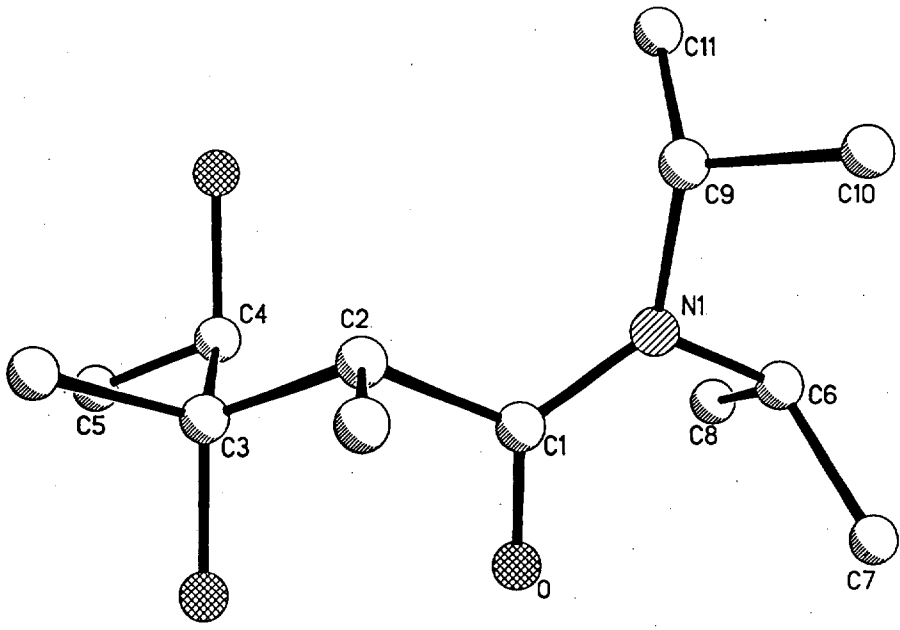
error= 9 ppm; IR (neat, cm^{-1}) 1710, C=O; 1634, C=O; 300 MHz NMR ($CDCl_3$, ppm) δ 4.18 (1H, sept, J= 6.8 Hz) 3.40 (1H, br s) 2.99-2.75 (2H, m) 2.50-2.21 (3H, m) 2.15-2.06 (1H, m) 1.97-1.86 (1H, m) 1.80-1.50 (2H, m) 1.40-1.30 (9H, m) 1.27-1.11 (1H, m) 1.22 (3H, d, J= 6.6 Hz) 1.02 (3H, d, J= 7.0 Hz).

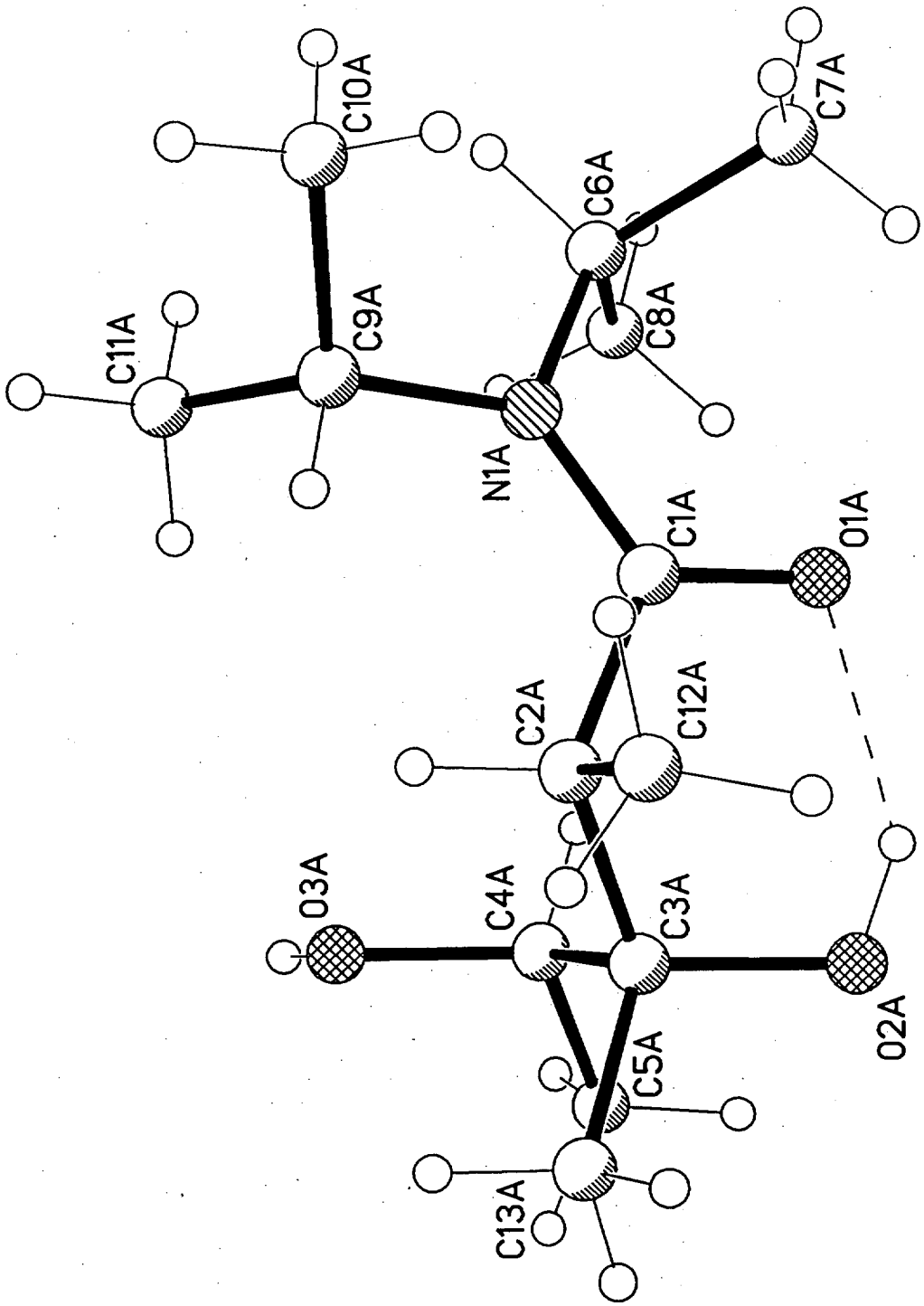
Lactone 30.[13a] To **27b** (13 mg, 0.06 mmol) was added 10% H_2SO_4 (0.16 mL, 0.28 mmol) and the mixture was refluxed 6.5 h. The cooled solution was diluted with 10 mL ether and then dried ($MgSO_4$) and evaporated (aspirator) to give 6 mg (80%) of **30**.[13a] ^1H NMR analysis indicated that this material was identical to that described by Eschenmoser, *et al.*[13a]

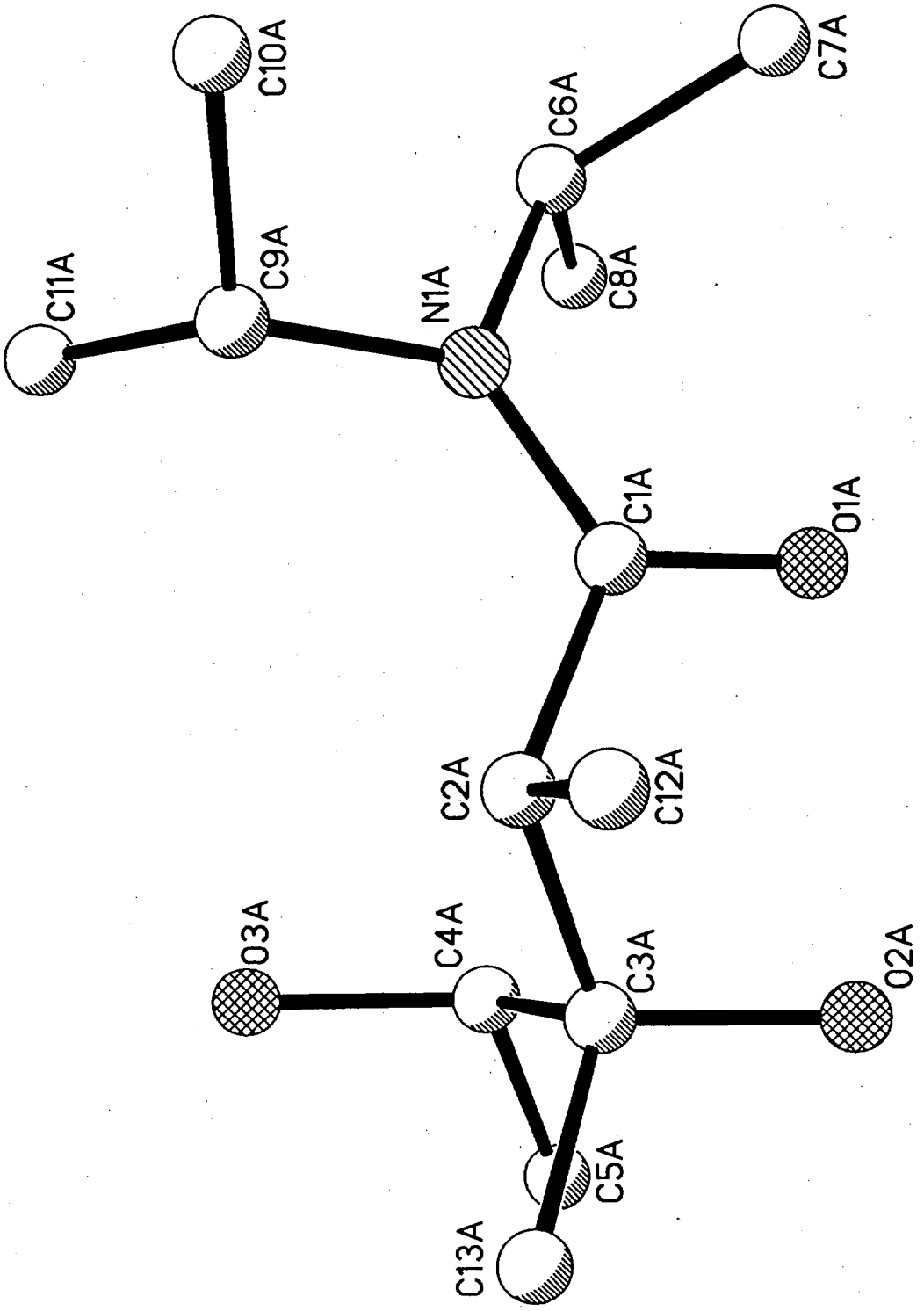
Lactone 31.[13a] To **28b** (4 mg, 0.02 mmol) was added 10% H_2SO_4 (0.15 mL, 0.27 mmol) and the mixture was refluxed for 6 h. The cooled solution was diluted with 10 mL ether and then dried ($MgSO_4$) and evaporated (aspirator) to give 2 mg of **31**. ^1H NMR analysis indicated that the lactone **31** and elimination product **12** were present in a 2:1 ratio. The lactone **31** was identical to that described by Eschenmoser, *et al.*[13a]

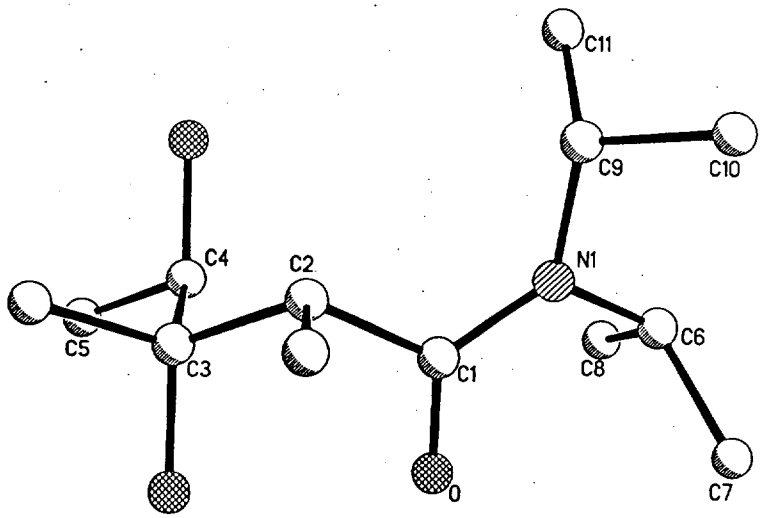
Lactone 32.[13b] To **29b** (48 mg, 0.19 mmol) was added 10% H_2SO_4 (0.53 mL, 0.94 mmol) and the solution was refluxed for 4 h. The cooled solution was diluted with 10 mL ether and then dried ($MgSO_4$) and evaporated (aspirator) to give 32 mg of a 1:2 mixture of **29b** and **32**. The residue was purified by preparative layer chromatography on EM silica gel 60 (20x20x0.1 cm), 1:1 hexane/ether eluent, to afford 15 mg (52%) of **32**. ^1H NMR analysis indicated that this material was identical to that described by Pitacco, *et al.*[13b]

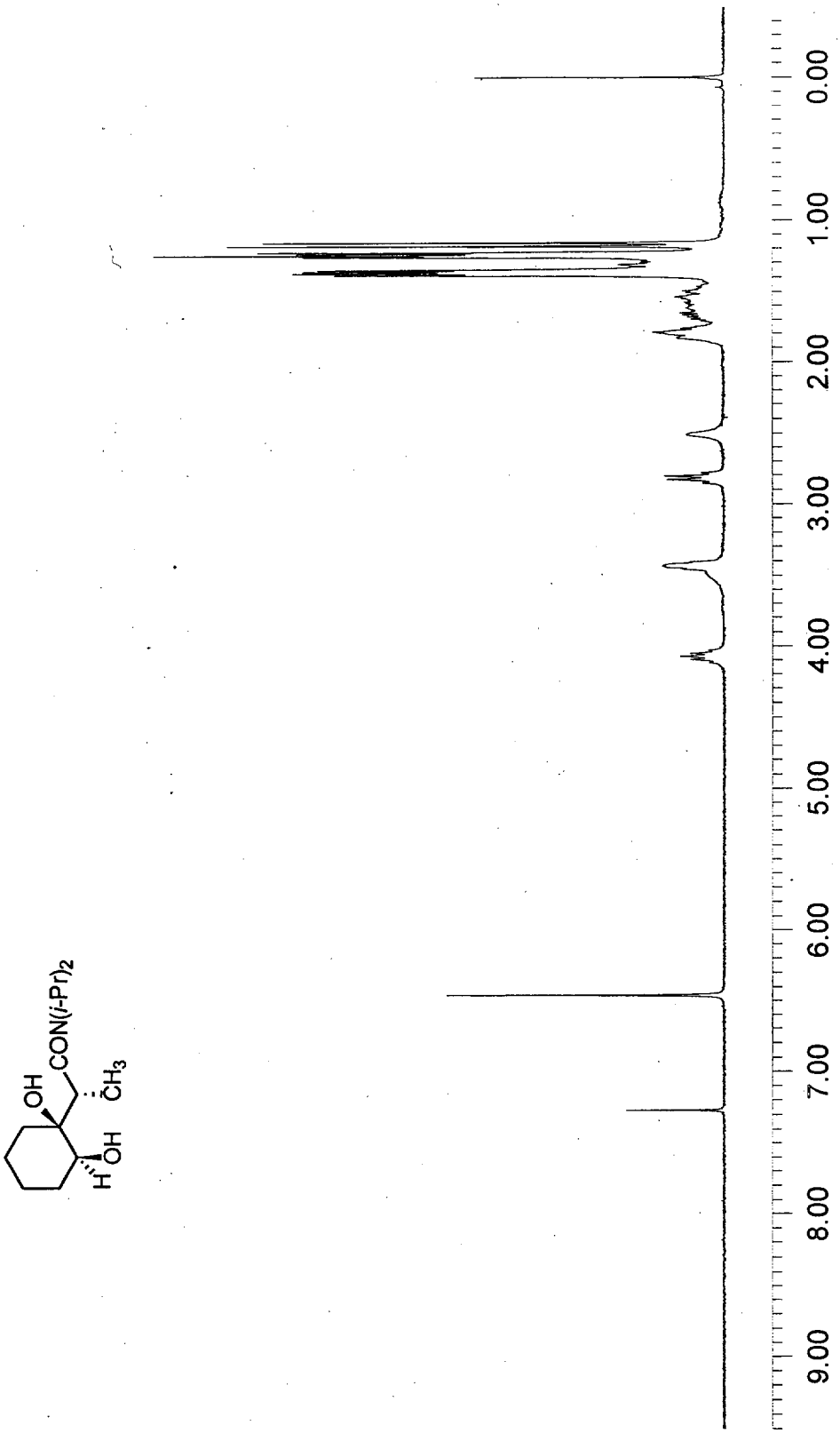

C11
C9
C10
N1
C4
C2
C6
C5
C3
C1
C8
O
C7

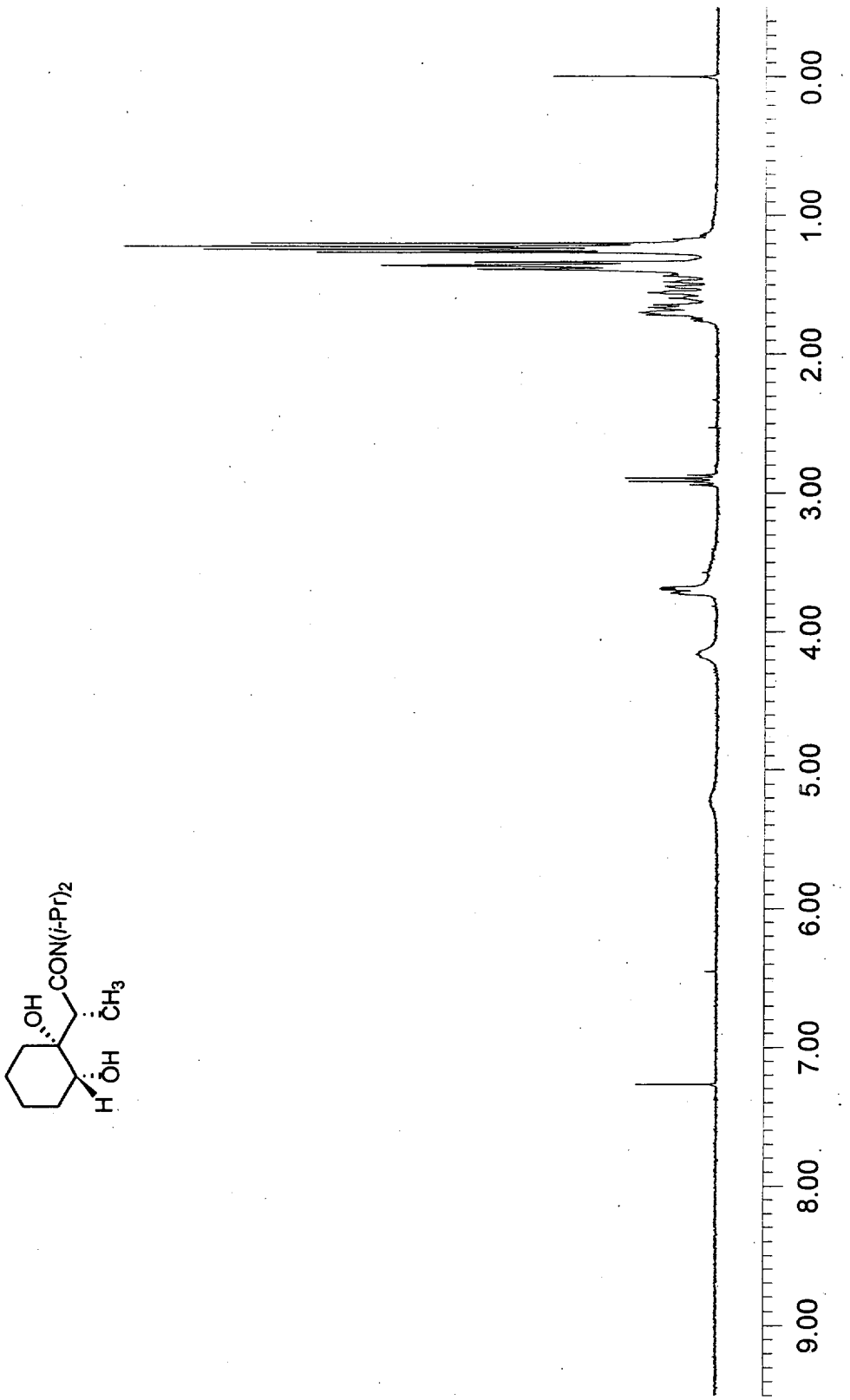

C11
C9
C10
N1
C4
C2
C6
C5
C3
C1
C8
O
C7

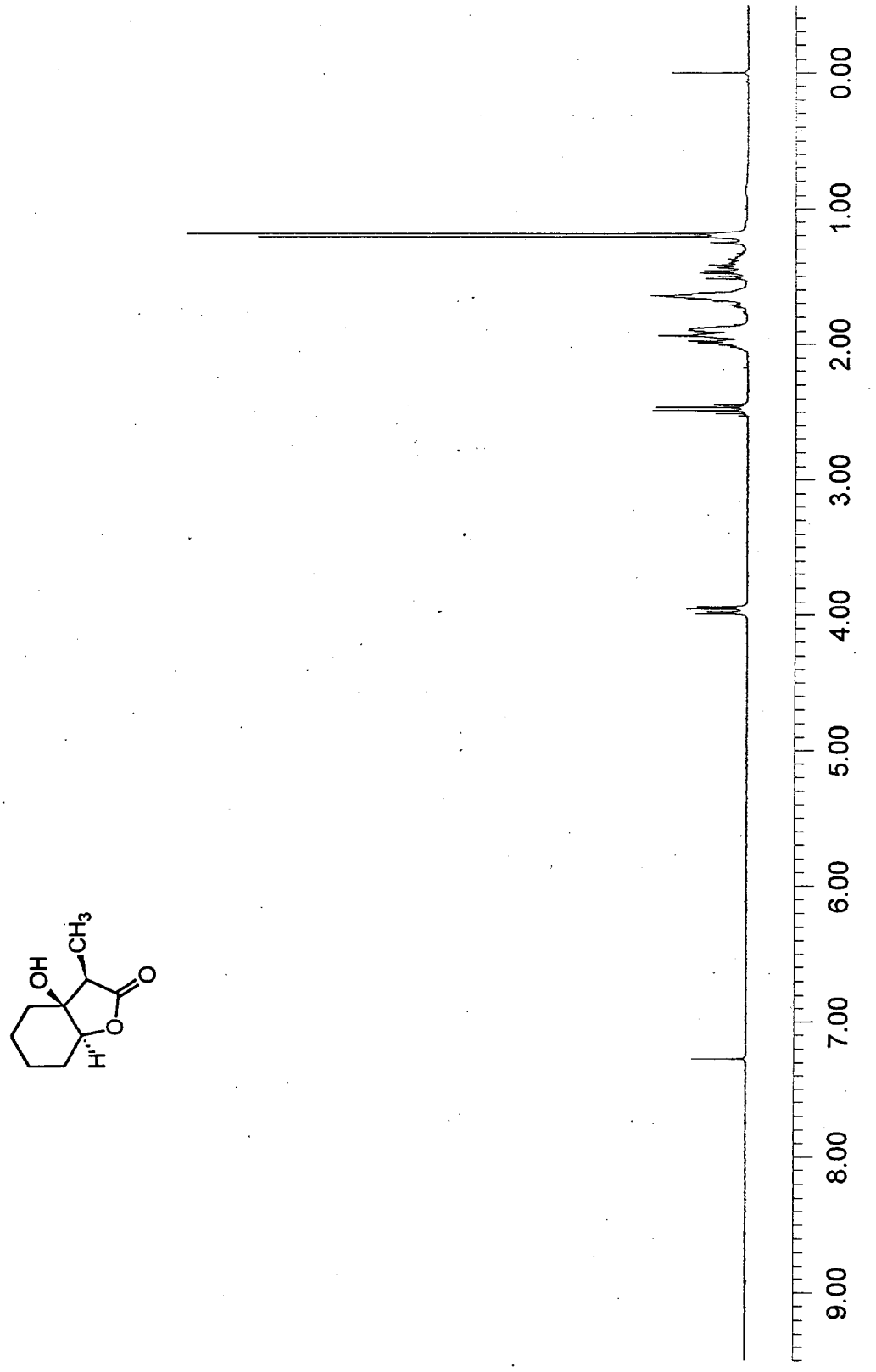

C10A
C7A
C6A
C11A
C9A
C8A
N1A
C1A
O1A
C2A
C12A
O3A
C4A
C3A
O2A
C5A
C13A

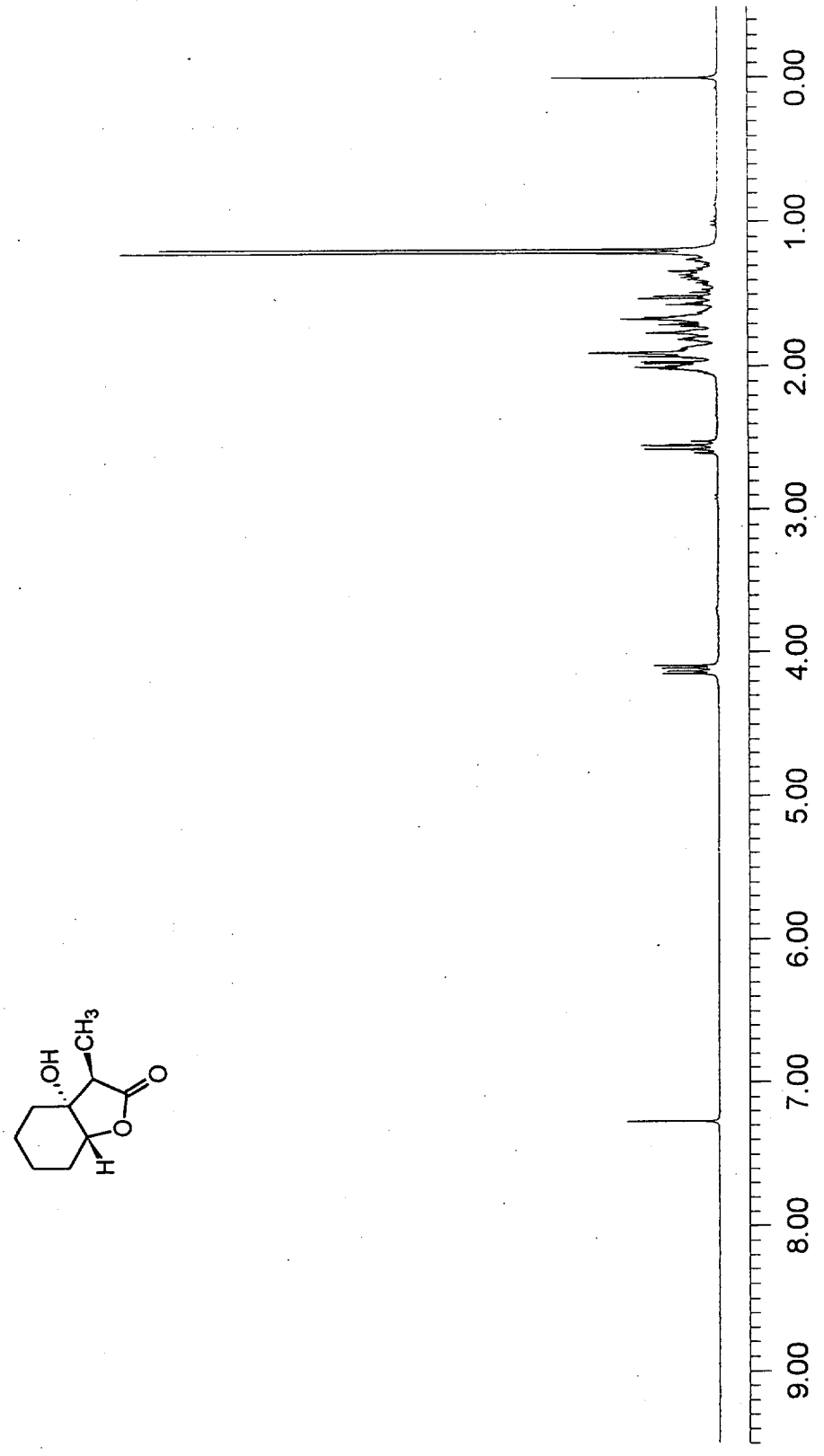

C10A
C7A
C6A
C11A
C9A
N1A
C8A
C1A
O1A
C2A
C12A
O3A
C4A
C3A
O2A
C5A
C13A

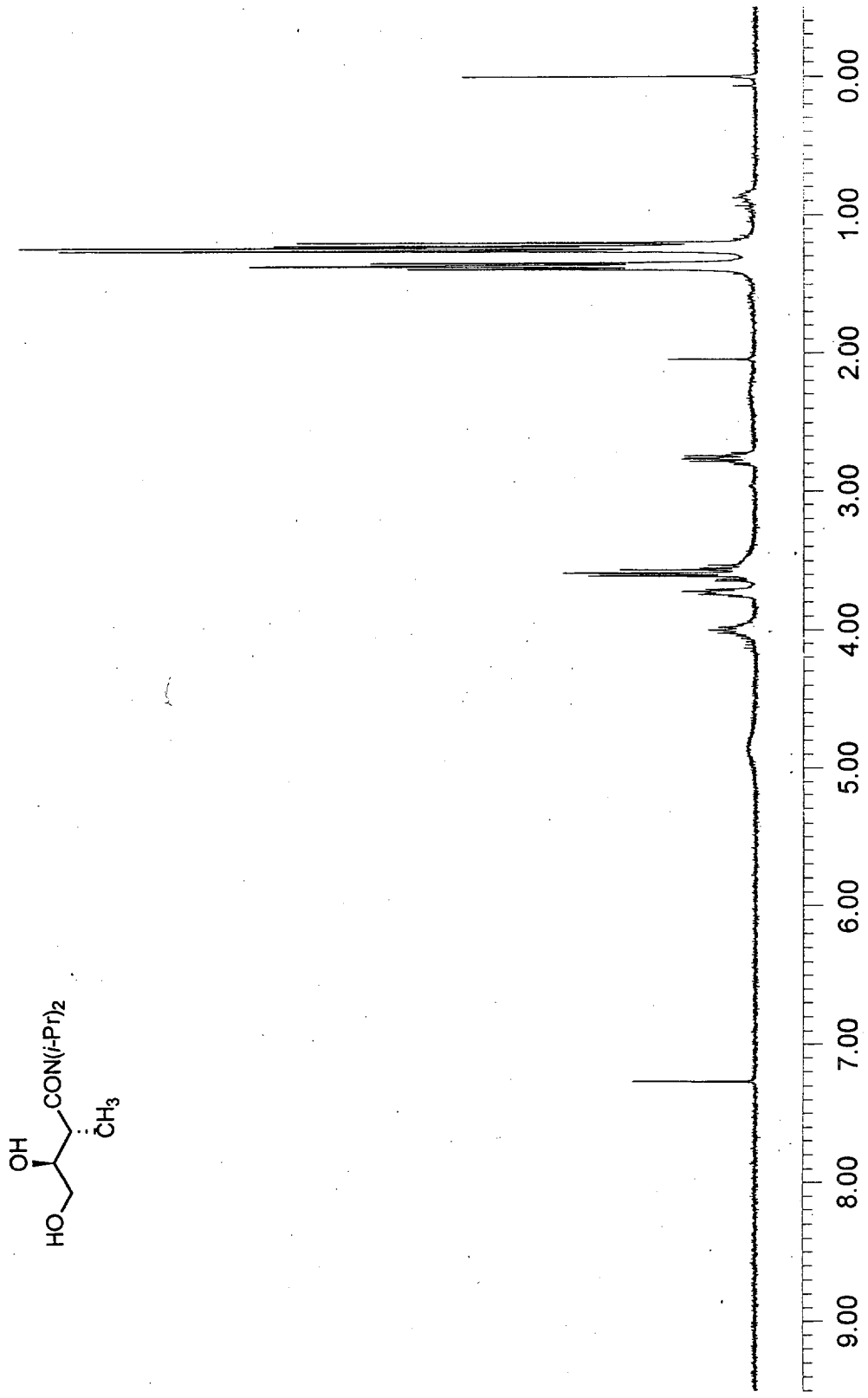

C11
C9
C10
C4
C2
N1
C5
C3
C1
C8
C6
O
C7

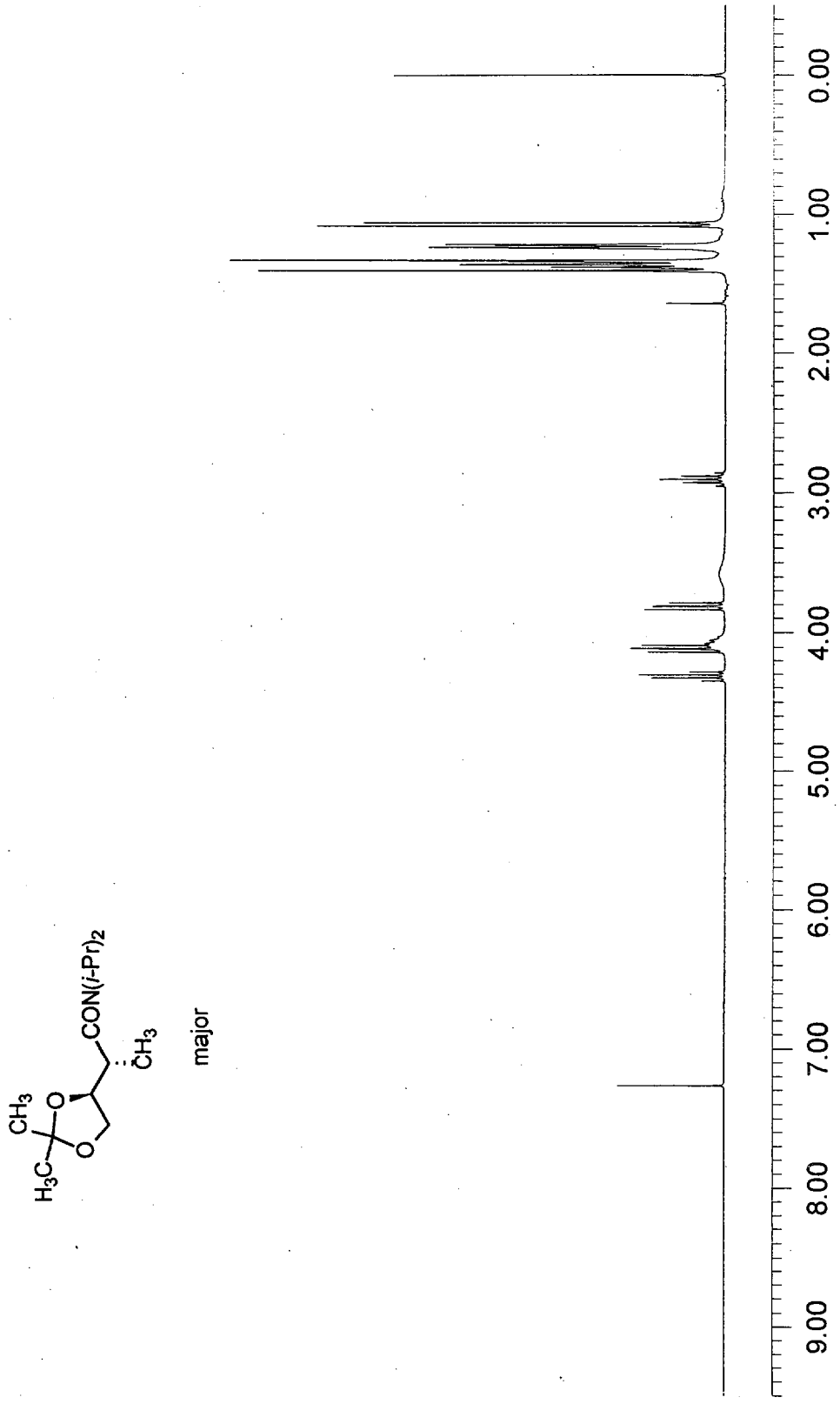


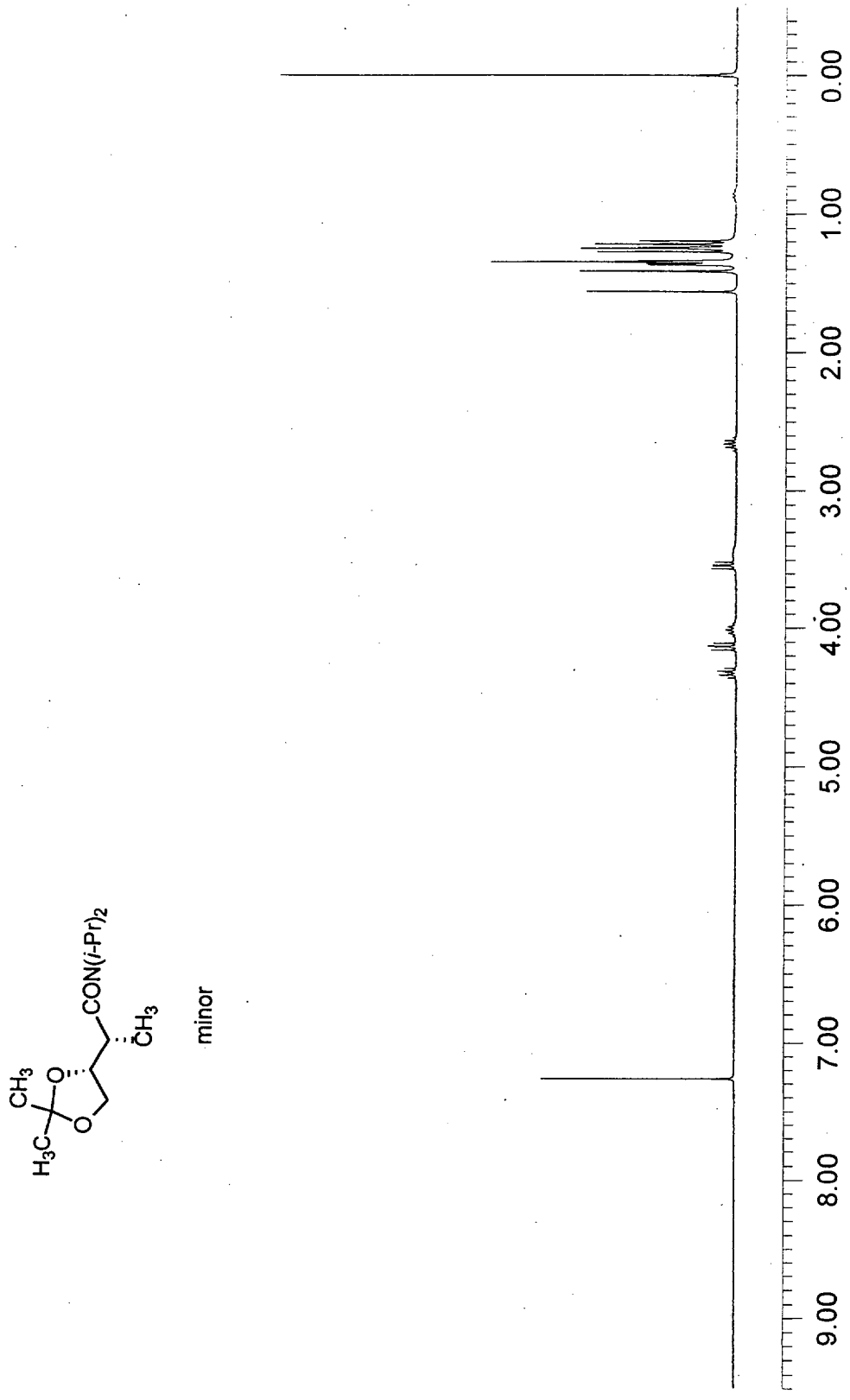

OH
CON(i-Pr)2
CH3
OH
H
0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00

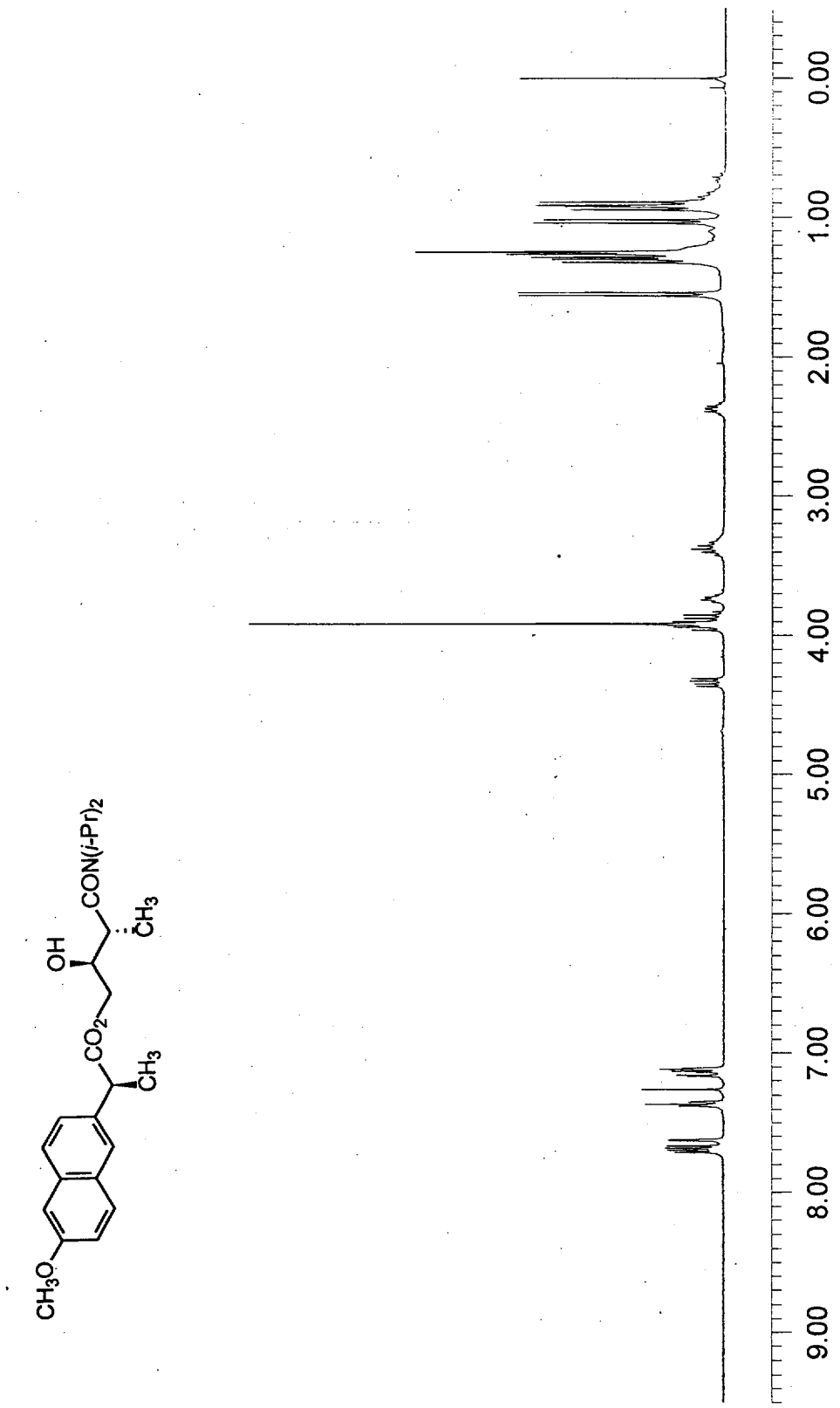


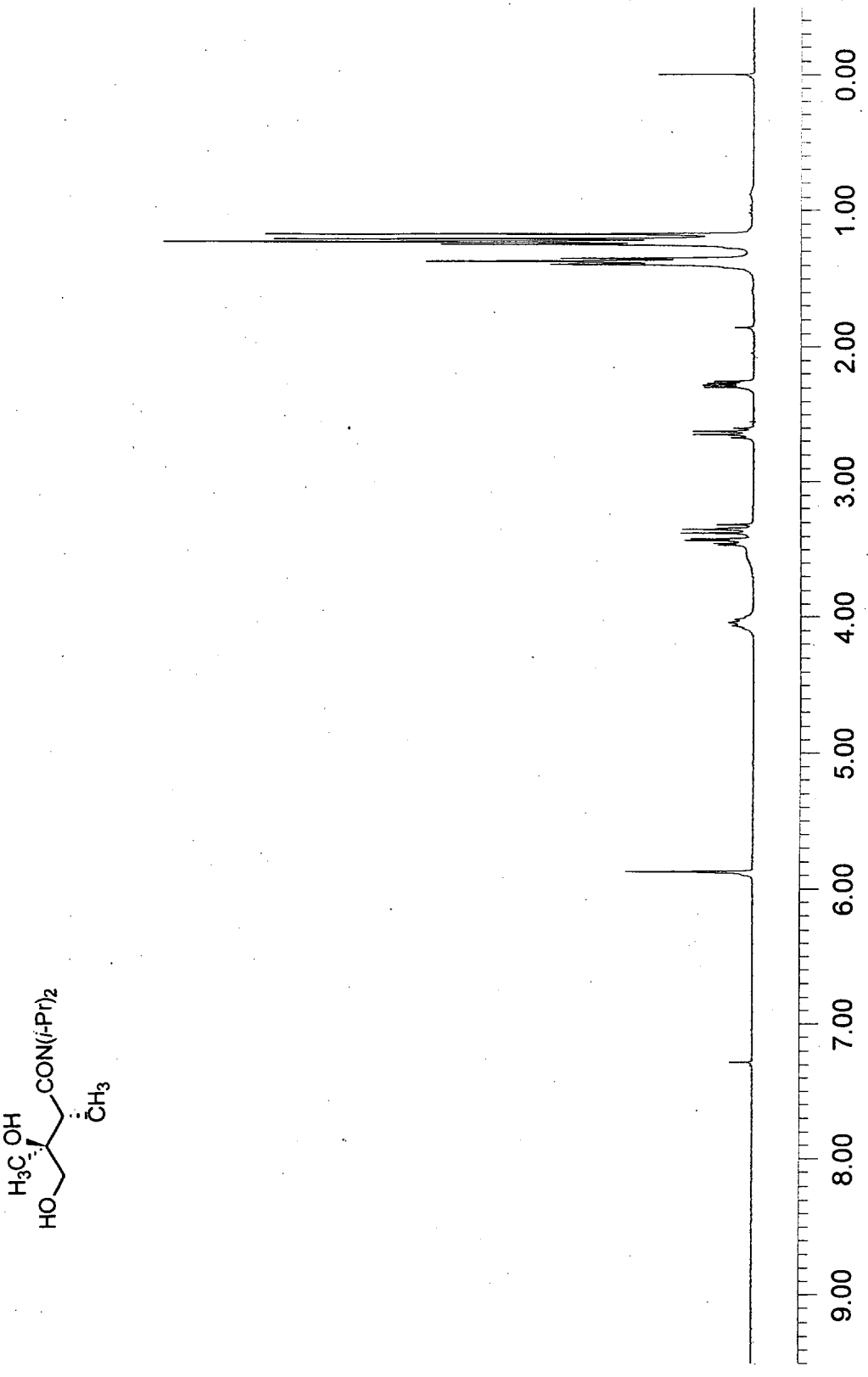

0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00
OH
CH3
O
O
H

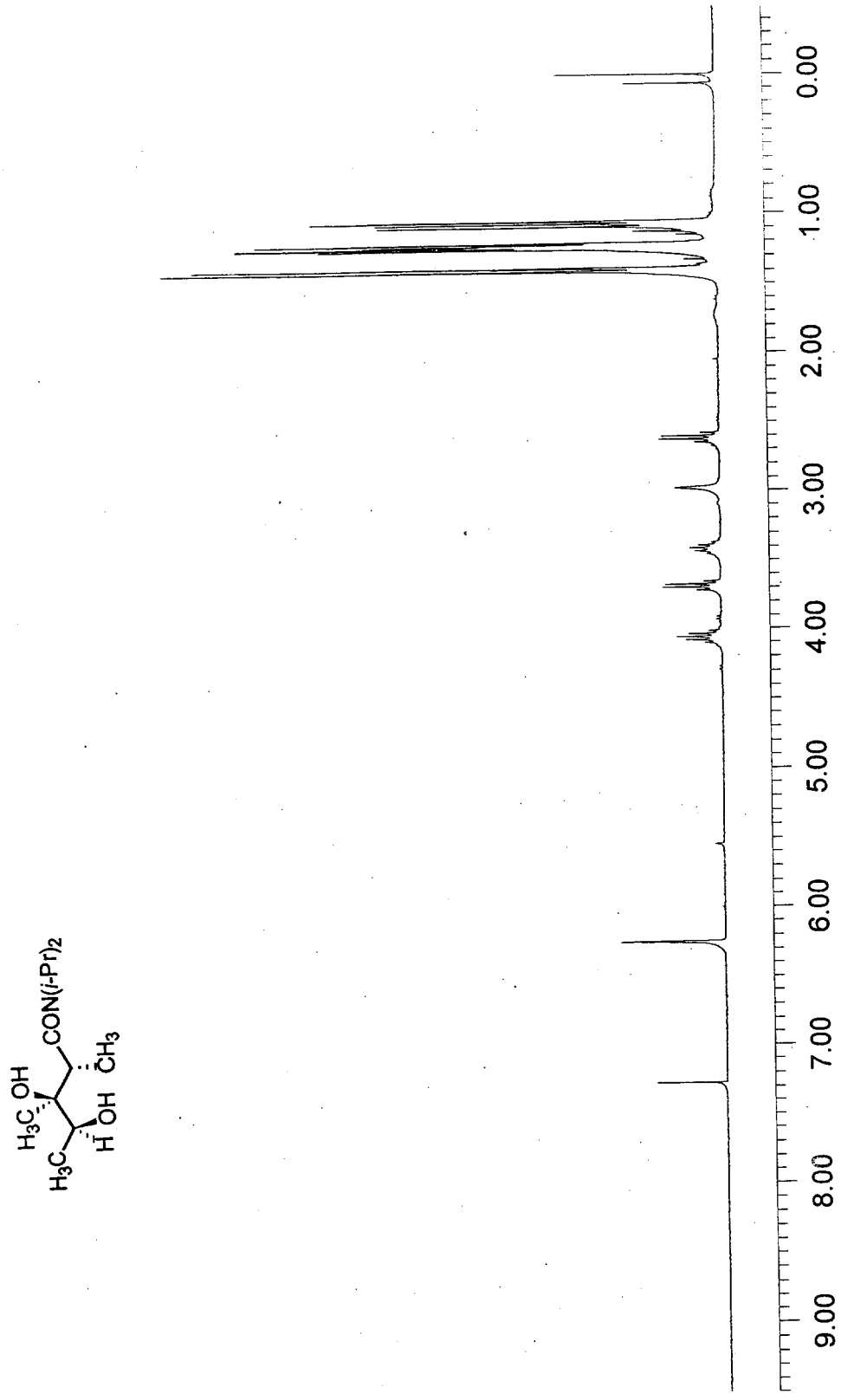

OH
CON(i-Pr)2
CH3
HO
0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00

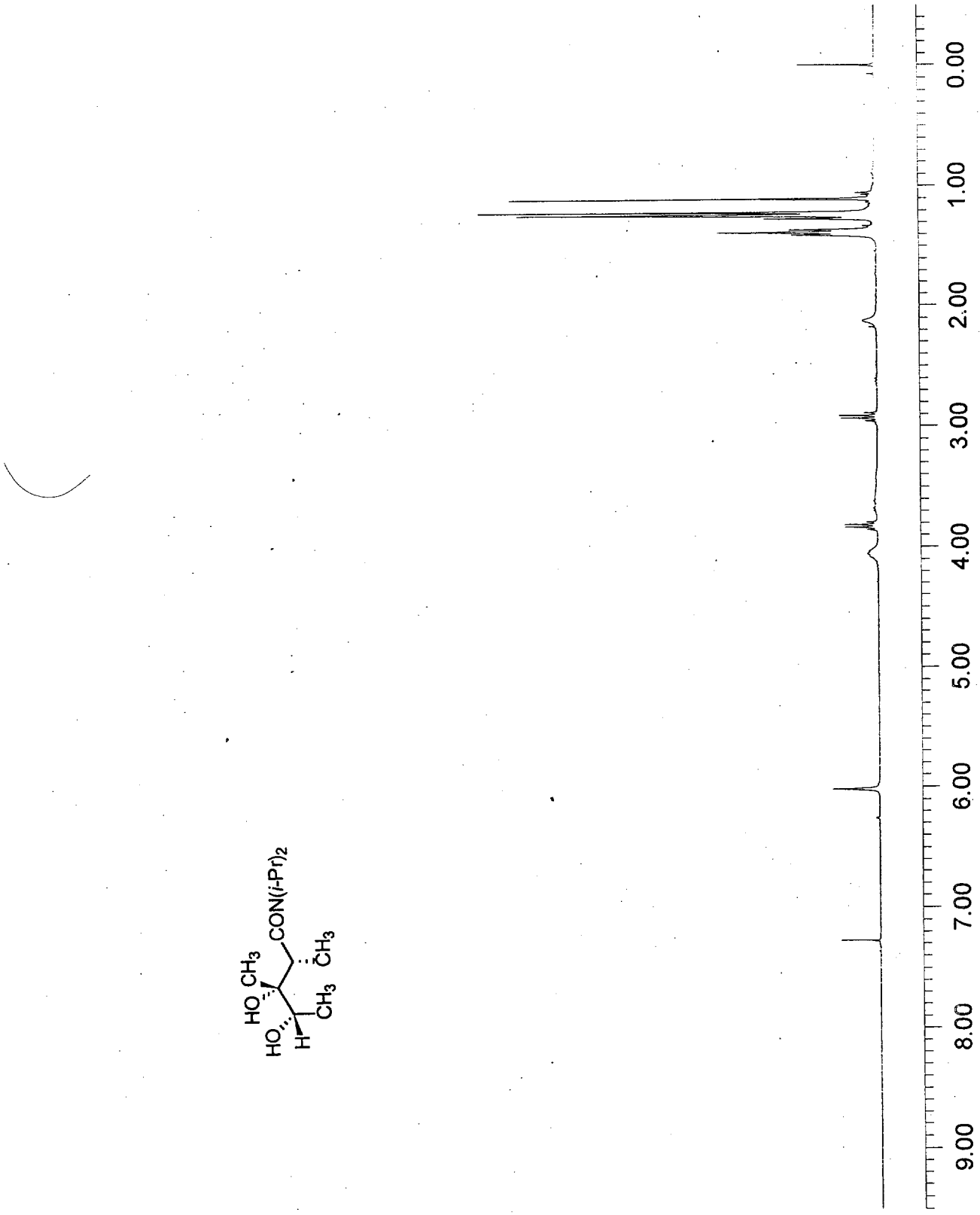


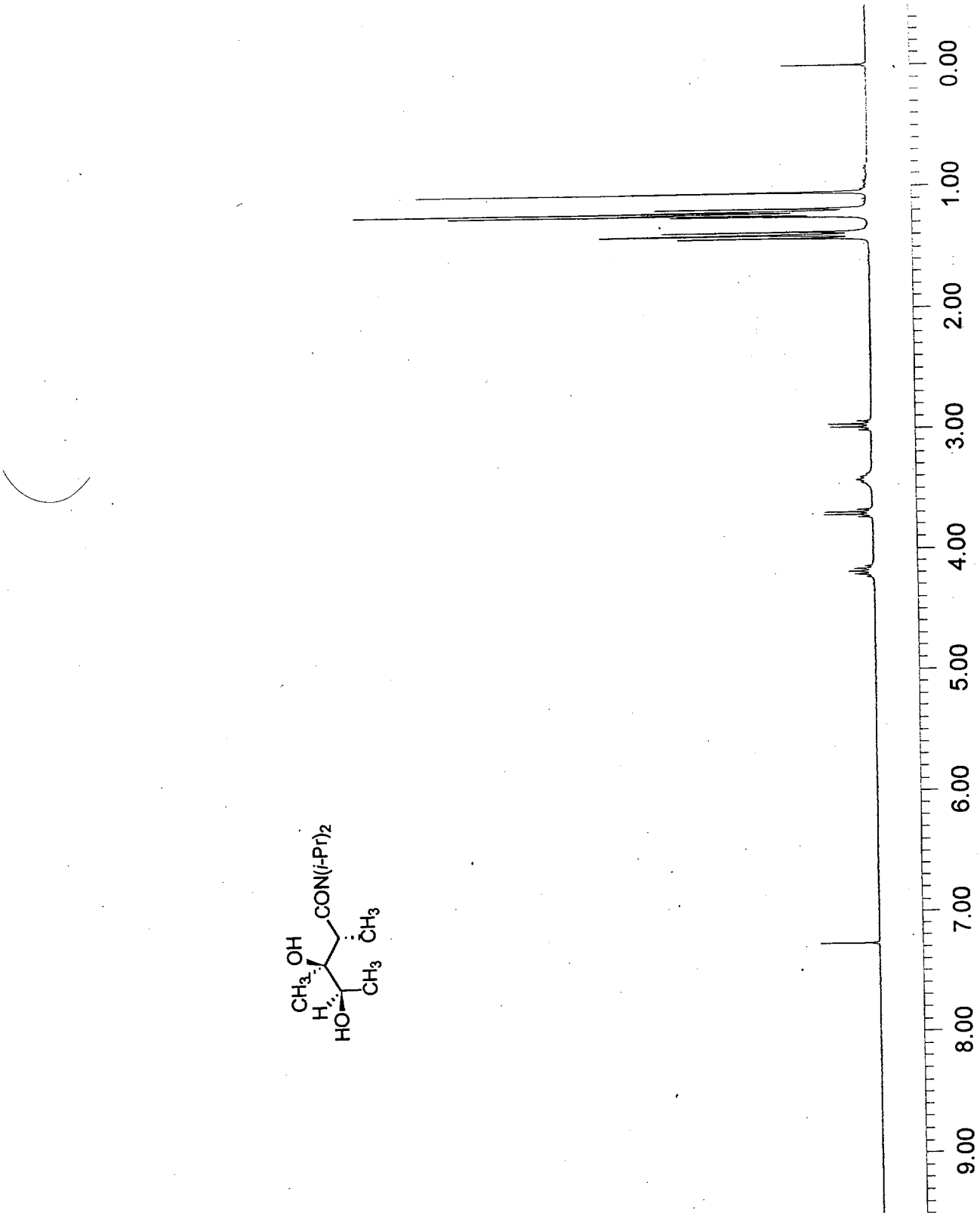

CH3
H3C
O
O
CON(i-Pr)2
CH3
minor
9.00
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00

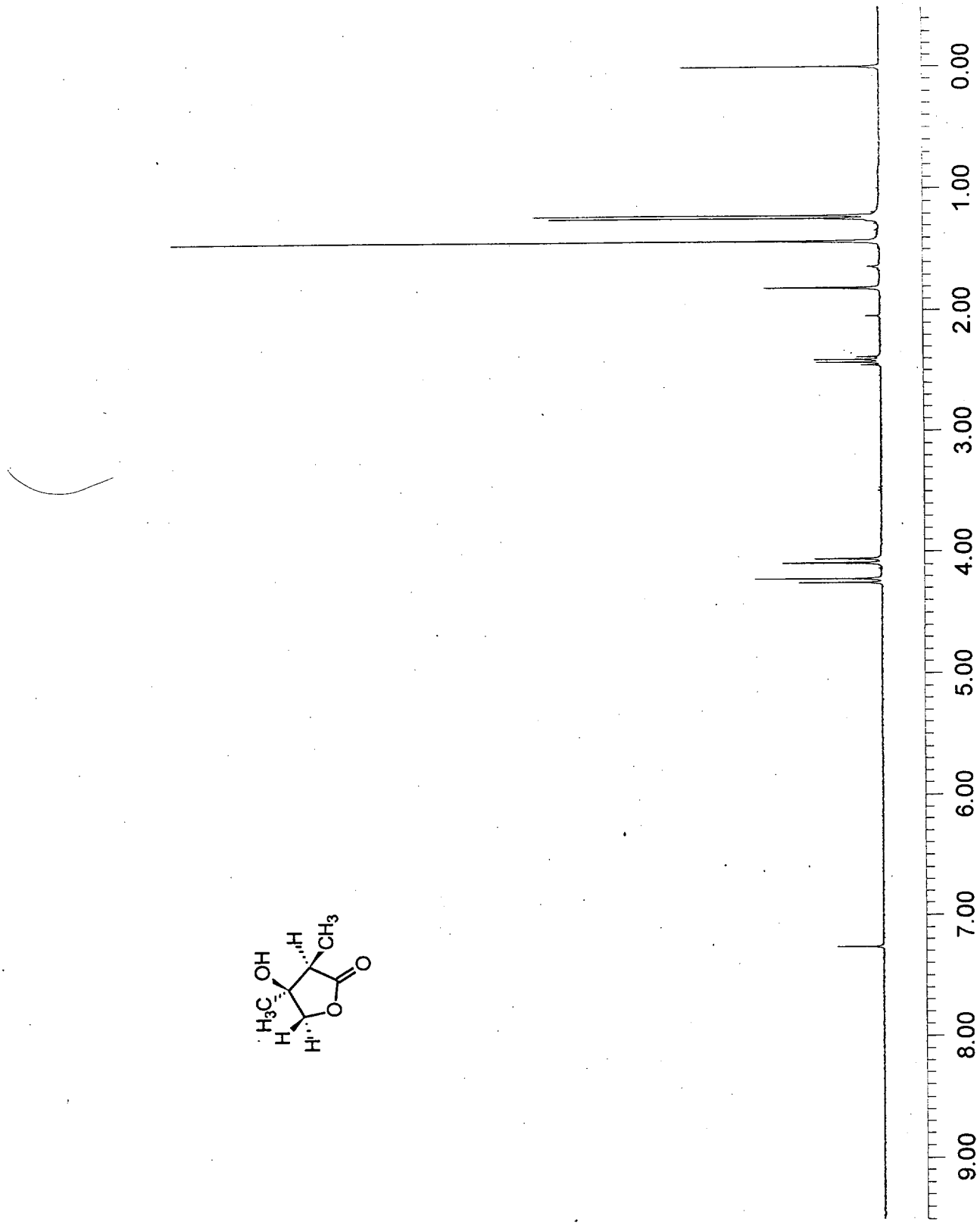


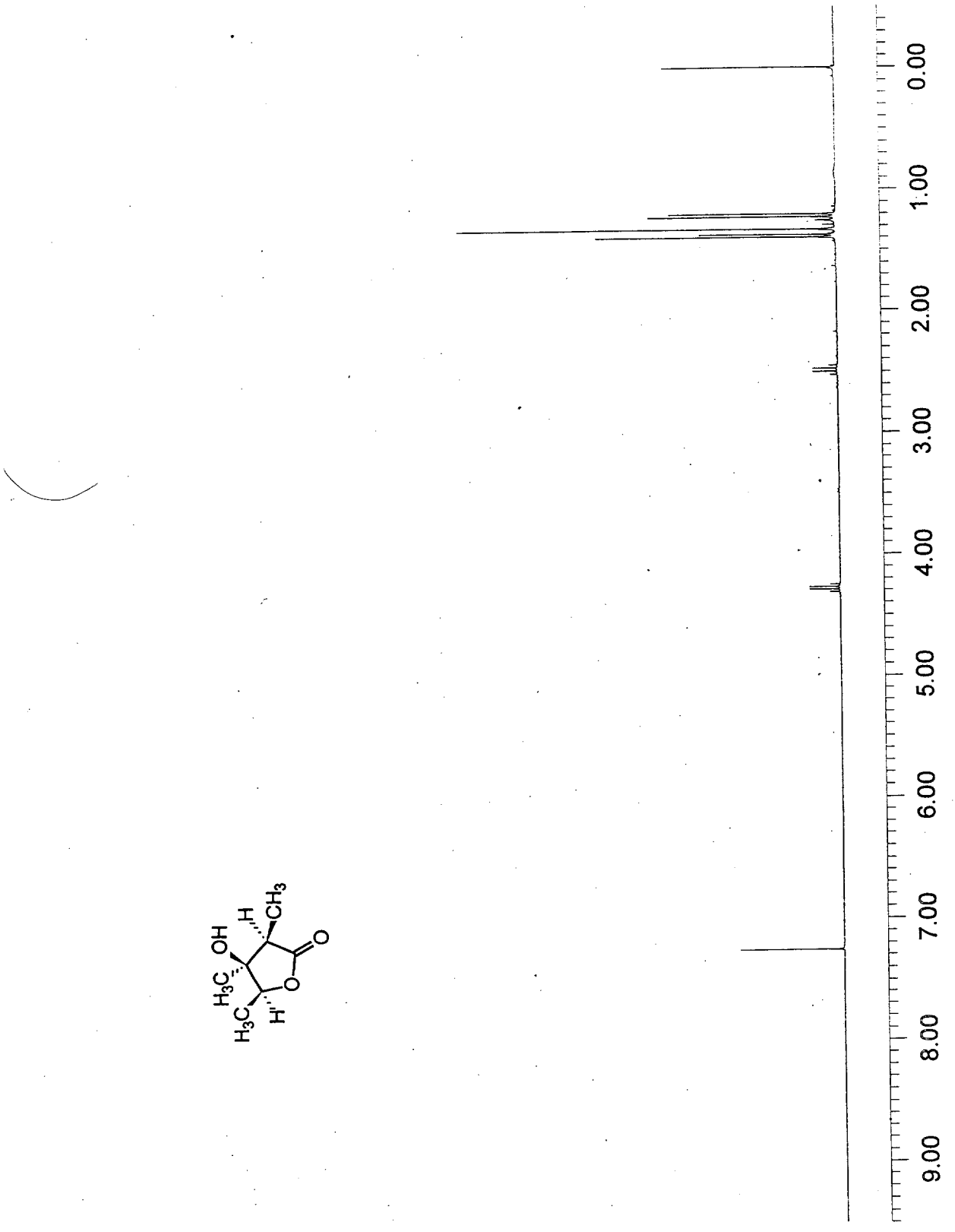


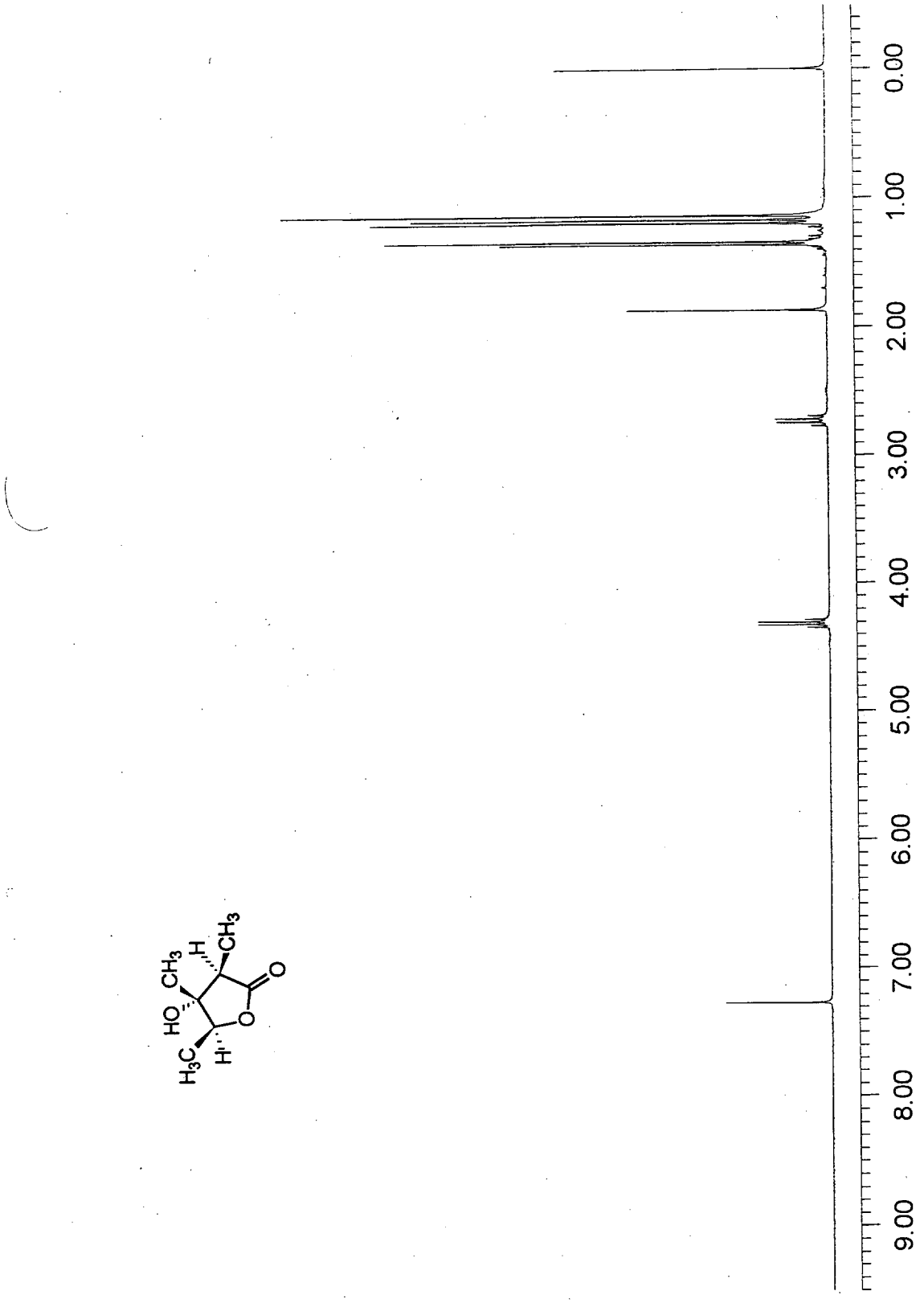


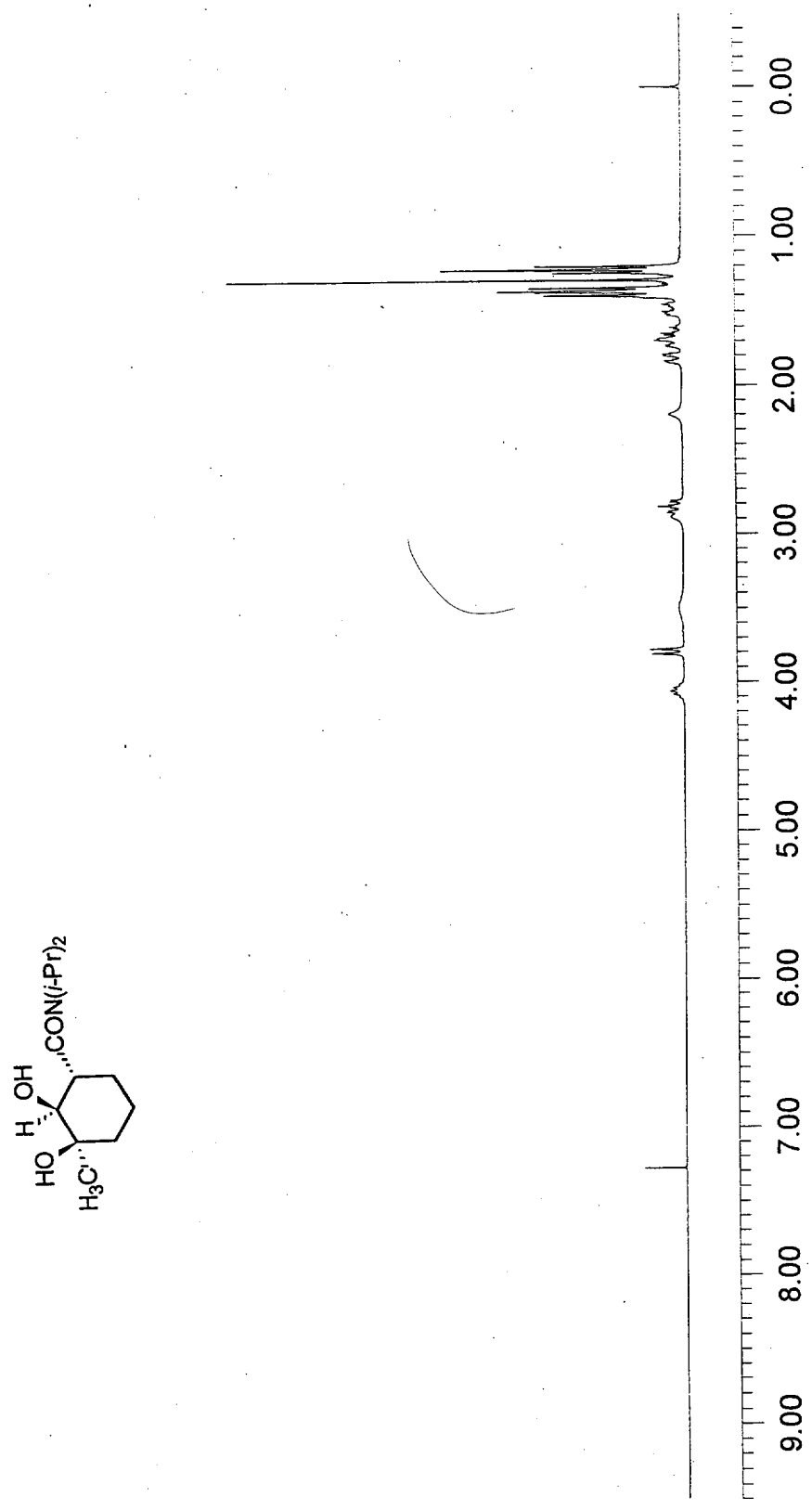

HO
CH3
HO
H
CH3
CH3
CON(i-Pr)2
9.00
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00

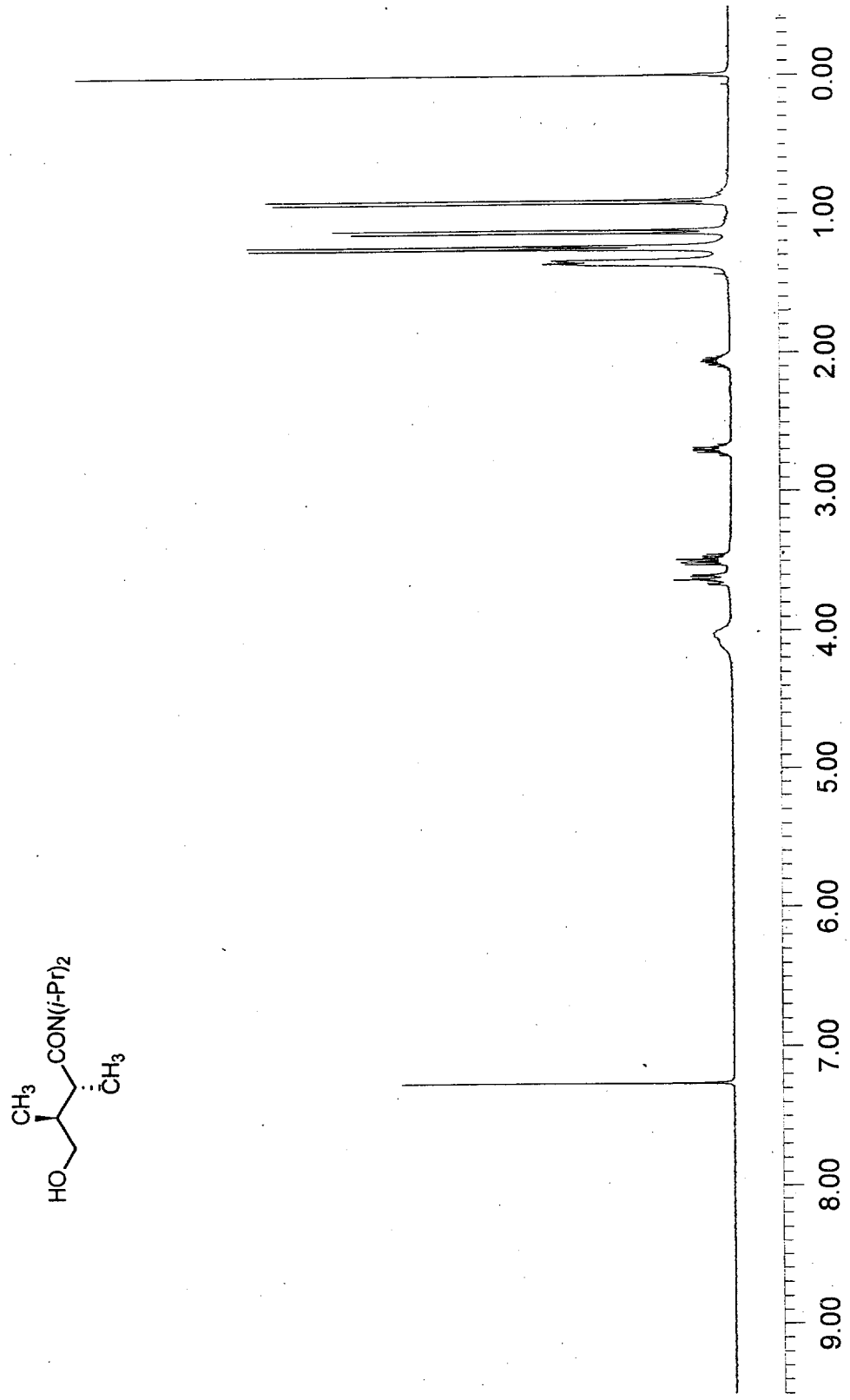


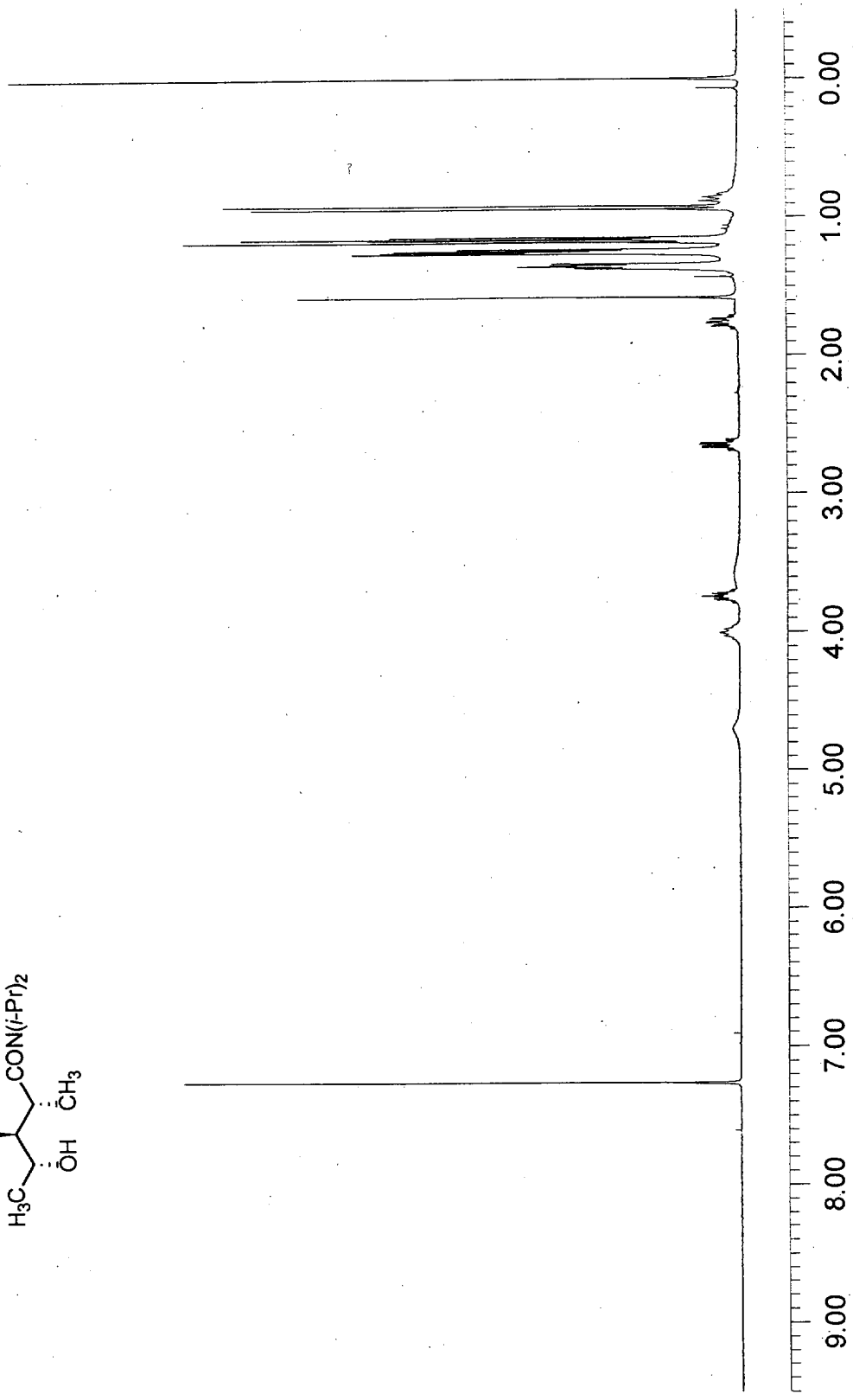


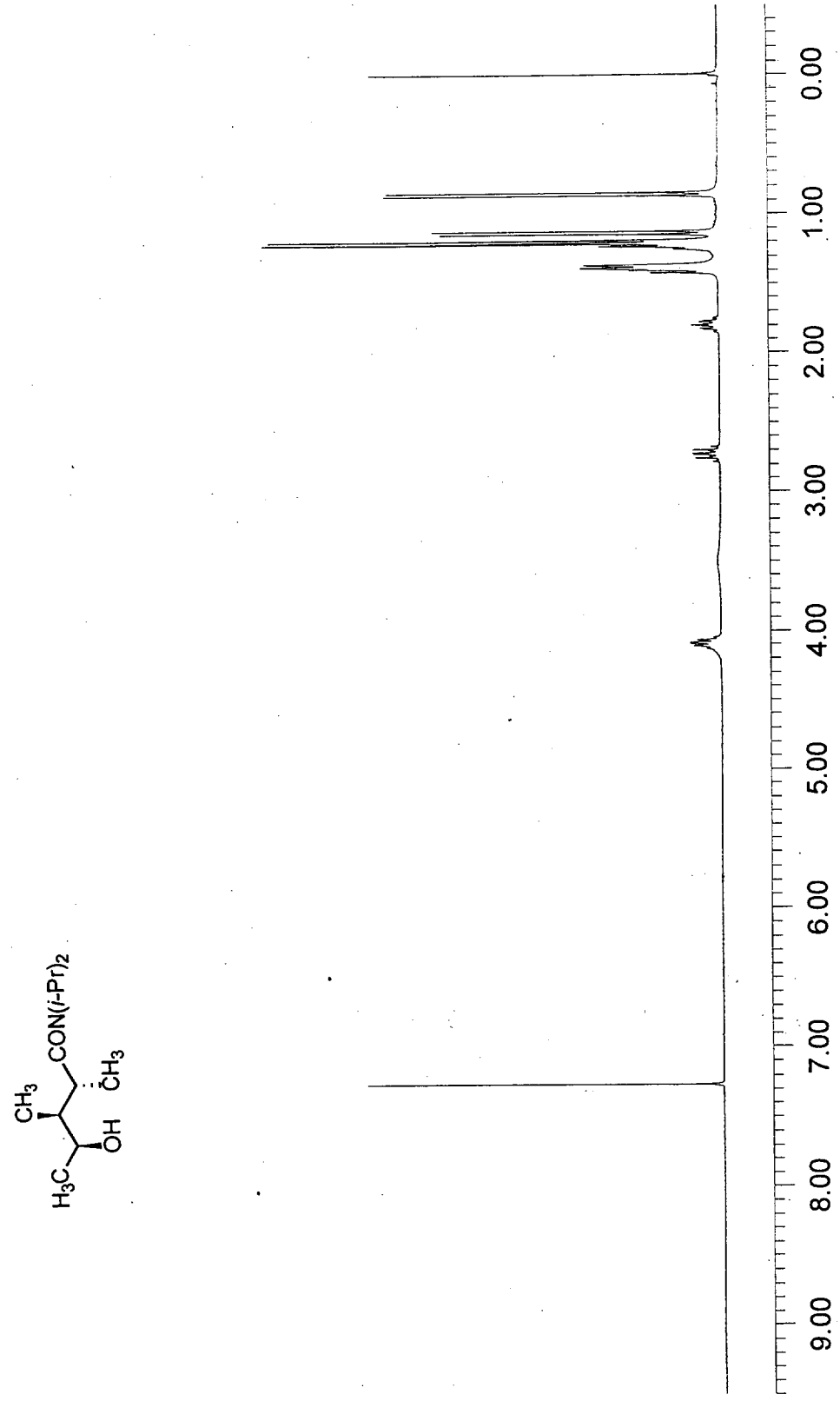

0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00
H
CH3
OH
H3C
O
H3C
H
O

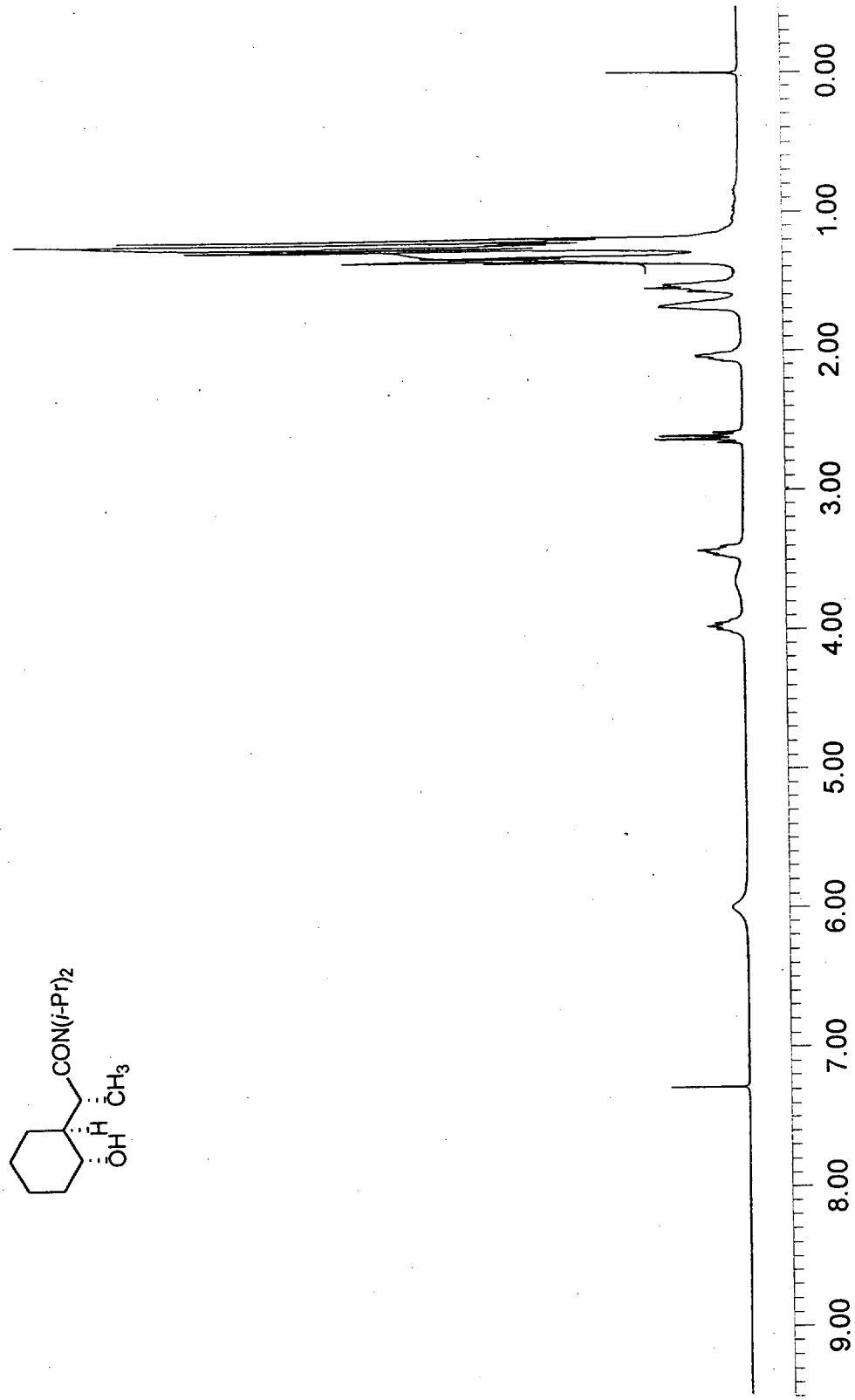

0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00
HO
CH3
H
CH3
O
O
H3C
H

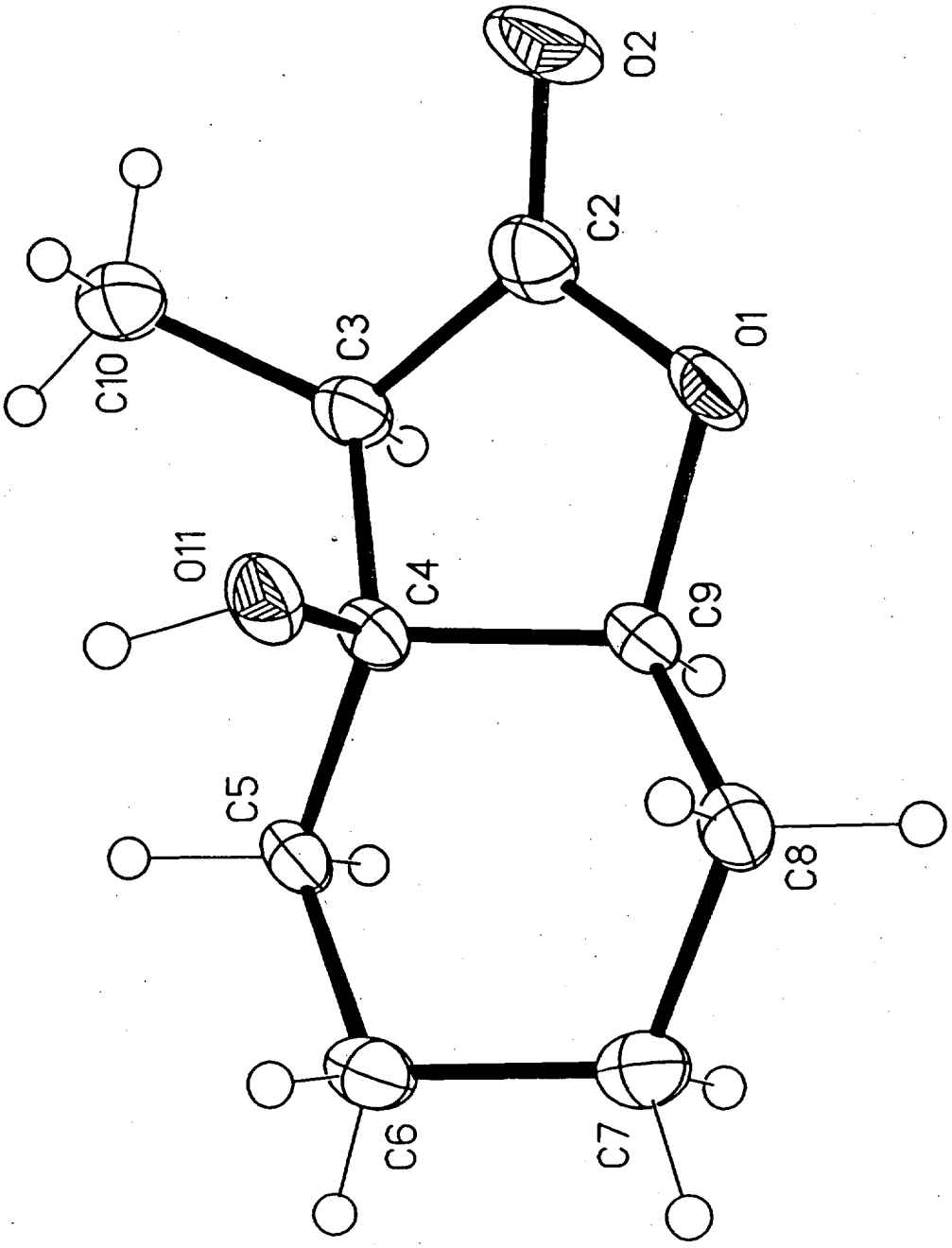


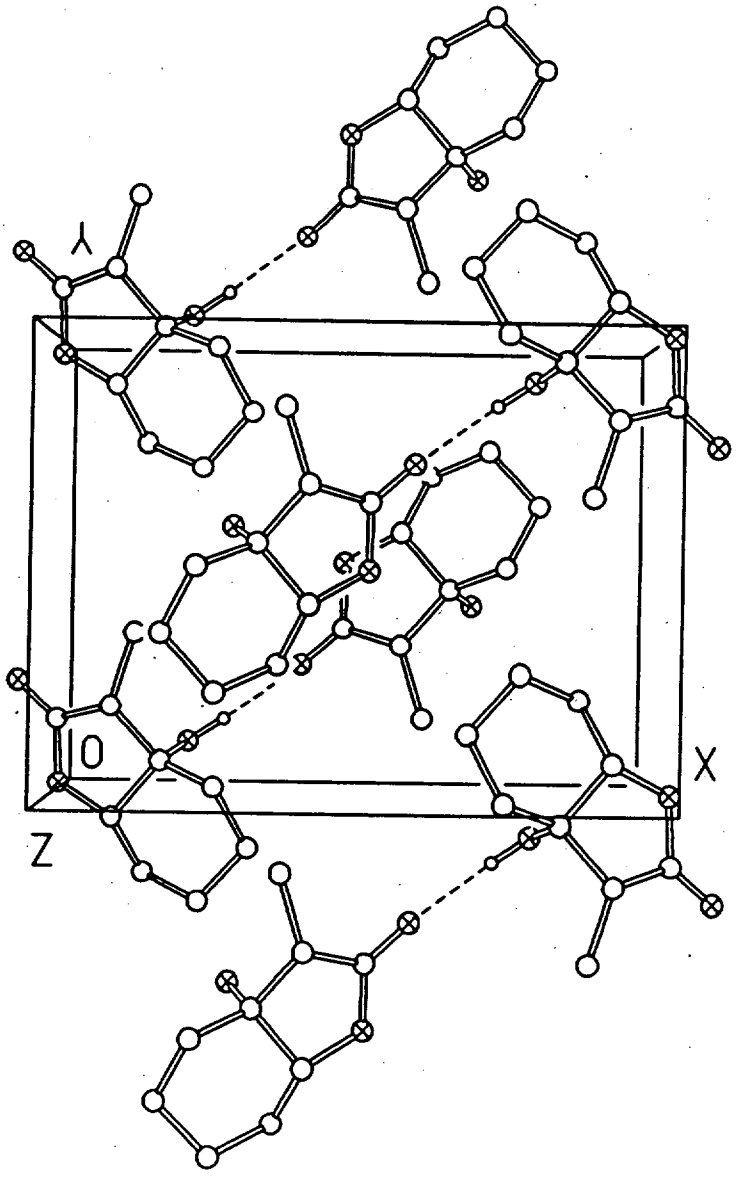



CH3
CON(i-Pr)2
CH3
OH
H3C
0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00


CH3
CON(i-Pr)2
CH3
OH
H3C
0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00




O2
C2
O1
C3
C10
O11
C4
C9
C5
C8
C6
C7


Y
O
X
Z